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THE RELATION OF EFFORT TO ATTACKS OF ACUTE MYOCARDIAL INFARCTION

LIEUTENANT COLONEL HERRMAN L. BLUMGART

Associate Professor of Medicine, Harvard Medical School (on leave of absence); Visiting Physician, Beth Israel Hospital (on leave of absence)

MEDICAL CORPS, ARMY OF THE UNITED STATES

In army experience the occurrence of acute myocardial infarction during or soon after strenuous effort is striking. The relation between effort and attacks of coronary occlusion or myocardial infarction has been the subject of considerable discussion because of the important clinical and other practical implications.[1] Thus, Master and his associates[2] analyzed the events preceding 530 attacks of coronary thrombosis and found that only 2 per cent followed unusual exertion, 5 per cent followed excitement and 37 per cent occurred during mild activity. They pointed out that, since half of the day of normal persons is spent in mild or moderate activity, one might well expect half of all attacks to occur during this period and concluded that effort is not a precipitating factor in causing myocardial infarction. These authors state that "although both angina pectoris and coronary artery thrombosis have the same underlying pathologic condition, namely coronary sclerosis, they differ entirely in respect to the exciting cause of the attack." Boas[3] as well as others[4] has challenged this point of view, stating that in his experience bodily effort directly may induce closure of a coronary artery with cardiac infarction or may initiate the syndrome of angina pectoris. Boas[5] states:

I fully agree with Master that coronary thrombosis very often occurs while the individual is at rest or asleep and that in many cases no antecedent injury or effort has taken place. But to argue from this that such accidents are not competent causes of coronary thrombosis appears incorrect. The fact that pneumothorax is due usually to pulmonary tuberculosis or to the rupture of an emphysematous bleb does not negate the fact that it may follow trauma to the chest; or that cerebral hemorrhage is caused usually by disease of the cerebral arteries that it may not be due to trauma to the head.

As Bean pointed out, the fact that most motor accidents do not occur at speeds of 70 miles an hour does not prove that such speed may not be concerned in some motor accidents.

Most military personnel are called on to undertake strenuous effort and, particularly in the instance of some officers from civilian life, such effort is often decidedly unaccustomed. It therefore might be anticipated that if effort and myocardial infarction were causally related an increased number of such cases might be witnessed in the Army. This is indeed the case. The medical officers at practically every one of the many hospital installations which I have visited have witnessed one or more such instances. In each case unequivocal electrocardiographic tracings of myocardial infarction were observed during life and/or an acute fresh occlusion of one of the three major coronary arteries was disclosed at postmortem examination. In the 8 cases in which electrocardiographic tracings were made, the changes were characteristic. In the 3 patients who died before such tracings could be made, fresh thrombosis of a coronary artery was observed in 2 and fresh subintimal hemorrhage in the other case post mortem. The following 11 cases were selected from a larger available series because of the adequate available data and because they illustrate the varying relation between effort and acute myocardial infarction:

CASE 1.—A major in the Field Artillery, aged 35, had had "gas" with epigastric and substernal distress for about eighteen months, precipitated by nervousness or anxiety, relieved by "belching" and occasionally by vomiting, but not related to exertion, eating or change in weather. On the afternoon before the day of admission he played baseball and hit a home run. As he reached the home plate "suddenly everything went black." He collapsed to the ground. He recovered sufficiently after five or ten minutes to get up and after half an hour walked to his quarters. At midnight he suffered severe substernal distress, dyspnea and cough. When admitted to the hospital at 3:30 a. m. he showed labored respiration, cyanosis and heart sounds of poor quality. The blood pressure was 95/78. The white blood cell count was 16,400. X-ray examination of the chest revealed evidence of pulmonary engorgement; there was no evidence of a pulmonary infarct. Electrocardiographic tracings were characteristic of cardiac anterior wall infarction. The patient rallied somewhat during the day under therapy including oxygen, but then pulmonary edema and dyspnea increased, the pulse became weak and the patient died eighteen hours after the ball game.

On postmortem examination of the heart, scattered foci of fibrosis were seen throughout the apex. and one area of old scar tissue measuring 2 cm. in diameter was evident in the left anterior ventricular wall. Above the latter area, acute necrotizing myomalacia was revealed grossly and microscopically. The left anterior coronary artery showed advanced arteriosclerosis with narrowing and one old healed occlusion. About 4 cm. from the origin of this artery, a fresh antemortem thrombus was found.

CASE 2.—A private aged 30 played volley ball immediately after calisthenics and developed substernal oppression and

1. Fitzhugh, G., and Hamilton, B. E.: Coronary Occlusion and Fatal Angina Pectoris: Study of the Immediate Causes and Their Prevention, J. A. M. A. **100**: 475 (Feb. 18) 1933. Sproul, John: A General Practitioner's Views on the Treatment of Angina Pectoris, New England J. Med. **215**: 443, 1936. Phipps, C.: Contributory Causes of Coronary Thrombosis, J. A. M. A. **106**: 761 (March 7) 1936. Paterson.[4] French and Dock.[6]

2. Master, A. M.; Dack, Simon, and Jaffe, H. L.: Factors and Events Associated with Onset of Coronary Artery Thrombosis, J. A. M. A. **109**: 546 (Aug. 21) 1937.

3. Boas, E. P.: Cardiac Infarction Induced by Unusual Effort, J. Mount Sinai Hosp. **7**: 307, 1941; Some Immediate Causes of Cardiac Infarction, Am. Heart J. **23**: 1, 1942; Angina Pectoris and Cardiac Infarction from Trauma or Unusual Effort.[5]

4. Paterson, J. C.: Relation of Physical Exertion and Emotion to Precipitation of Coronary Thrombi, J. A. M. A. **112**: 895 (March 11) 1939. French and Dock.[6]

5. Boas, E. P.: Angina Pectoris and Cardiac Infarction from Trauma or Unusual Effort, J. A. M. A. **112**: 1887 (May 13) 1939.

unusual dyspnea. He experienced persistent weakness for two days following this episode and then developed acute dyspnea, orthopnea and chest pain. Physical examination on admission disclosed orthopnea, dyspnea, ashen gray cyanosis, cold sweat, heart rate 100 per minute, weak cardiac sounds, gallop rhythm and a blood pressure of 124/80. The patient gradually improved during the following four days but showed evidence of pulmonary edema. Serial electrocardiographic tracings revealed progressive changes characteristic of anterior wall infarction. He gradually improved and was discharged from the hospital twelve weeks later.

CASE 3.—A private aged 37 experienced occasional vague substernal discomfort, unrelated to exertion, during ten days before admission. On the day before admission he ran a distance of 1 mile, immediately following which he experienced persistent weakness, which continued until he fell asleep. At 2 a. m. he was awakened by severe substernal pains, with numbness radiating to the left arm; he felt prostrated and had drenching cold sweat. He was admitted immediately to the hospital. Physical examination revealed evidence of shock with rales at both bases. The heart rate was 120 per minute. During the next three days the substernal oppression gradually subsided and the patient made an uneventful recovery. Serial electrocardiographic tracings showed pronounced changes characteristic of anterior wall infarction.

CASE 4.—A captain in the Signal Corps, aged 41, collapsed while on a hike and was dead on arrival at the hospital. Examination of the heart showed advanced arteriosclerosis of the left coronary artery and a fresh complete occlusion of the right coronary artery caused by friable atheromatous material.

CASE 5.—A first lieutenant in the Motorized Division, aged 26, while engaged on maneuvers during the night complained that he was dizzy and felt sick. He was taken to a nearby house, became acutely dyspneic and died within a few minutes. Examination of the heart revealed a fresh thrombus in one of several anomalous subdivisions of the right coronary artery. Old fibrotic changes were evident on the posterior wall of the left ventricle near the base.

CASE 6.—A captain in the Transportation Corps, aged 34, had felt perfectly well and was running an obstacle course, toward the end of which he had to scale a 12 foot wall. He felt perfectly well when he came to this obstacle. He failed to swing over it on the first attempt. On the second attempt he suddenly developed sharp chest pain, felt exhausted, had to gasp for breath, and broke out in profuse perspiration. The pain was initially substernal but soon radiated over the entire anterior chest and to the shoulders and arms. The substernal pain, very severe, subsided considerably during fifteen minutes and he finished the course without scaling the wall. At the end of about two and one-half hours the substernal distress disappeared entirely. Thereafter he repeatedly noted shortness of breath and mild substernal pain on exertion, disappearing in about five minutes on rest. He did not seek medical advice. These symptoms persisted and he had one severe attack following strenuous effort and was finally hospitalized. Physical examination showed a normal sized heart. The blood pressure was 106/84. Electrocardiographic tracings showed the characteristics in the first and fourth leads of a previous anterior wall infarction.

CASE 7.—An infantry colonel aged 56 had been assigned to sedentary duties for a period of two years and was then transferred to an infantry division for training and shipment overseas. To qualify for overseas duties he was required to complete the run of an obstacle course in a given period of time. Immediately after completion of the qualifying run, while taking a shower, he was seized with severe substernal pain and choking sensations and collapsed. He was immediately taken to the hospital. The findings on physical examination and the electrocardiographic tracings were characteristic of acute myocardial infarction. He made an uneventful recovery and was retired because of arteriosclerotic heart disease.

CASE 8.—A captain aged 47 was seized with precordial discomfort immediately after exercise in the gymnasium. He was advised to see a medical officer but did not do so despite the fact that he continued to have considerable precordial discomfort during the night. He sought medical advice the following afternoon. The electrocardiographic tracings were equivocal, and he was asked to exercise jumping on one foot while another electrocardiographic tracing was taken. Directly following this he collapsed and went into severe shock. He was then first seen by one of the officers in the medical service, who made a diagnosis of coronary thrombosis. The heart rate was slow, gallop rhythm was evident and the blood pressure was 100/60. His condition was critical, but under appropriate therapy he improved and eventually recovered. Serial electrocardiographic tracings were characteristic of posterior wall infarction.

CASE 9.—A staff sergeant in the Coast Artillery, aged 56, died suddenly during a tactical march with his unit. Postmortem examination revealed arteriosclerosis of all three coronary arteries. In the wall of the left anterior descending artery "areas of fresh hemorrhagic extravasation and mixed round cell infiltration" were observed.

CASE 10.—A first lieutenant in the military police, aged 44, returned from a 20 to 25 mile march, felt well, ate dinner and one hour later suddenly experienced substernal oppression. He collapsed, was unconscious for several hours and was transported to the hospital. He then experienced severe precordial pain, choking sensations and dyspnea. He gradually improved and was retired from the service. Serial electrocardiographic tracings were characteristic of posterior wall infarction.

CASE 11.—A private aged 31 had been a clerk in civilian life and after induction was assigned to similar duties in a finance department at a port of embarkation. He was then transferred for basic training. As part of the program of basic training he engaged in vigorous swimming in very cold water with his platoon for one and one-half hours. He got out of the water at 11:15 a. m. and while marching back to his barracks at 11:25 was suddenly seized with extremely severe viselike retrosternal pain, which, to quote his words, was "almost more than I could stand. I do not know how I made it back." He nevertheless marched the three fourths of a mile to his barracks, went to bed and was pale, drenched in cold sweat and dyspneic. The severe pain, after persisting one and one-half hours, subsided somewhat and he was admitted to the hospital. Physical examination revealed impending shock. But he rallied under appropriate therapy. The substernal distress disappeared after four days. Serial electrocardiographic tracings were characteristic of posterior wall infarction.

COMMENT

The question of the relation of effort to acute myocardial infarction is of considerable practical as well as theoretical importance. Legal decisions in civilian life and the line of duty determination in military service are often vitally affected. In case 7, for instance, although the officer had been in service for two years, it was initially decided that effort bore no relation to the attack of acute myocardial infarction and the line of duty determination was "no." Recognition of the relation of effort to acute myocardial infarction may be of great importance in diagnosis as well as in proper clinical management. Thus, failure to recognize the interrelation between effort and acute myocardial infarction in case 8 resulted in the continuation of exercise by the patient and even a request by a medical officer to undertake the effort of an exercise tolerance test.

The clinical experience illustrated by the foregoing cases emphasizes certain hitherto established facts which are not sufficiently kept in mind. The quality of cardiac pain is mimicked with fidelity by disease of other organs, and therefore a diagnosis of noncardiac disease is often mistakenly made. Clinical experience in the Army, as well as in civilian life, is in accord with that

of French and Dock,[6] who state that less than half of those who mentioned prodromal symptoms sought professional advice and that only 1 of the 14 cases with symptoms which suggested this condition had received a correct diagnosis and been treated before the fatal attack. In their communication, which has appeared since the present study was undertaken, they analyzed the findings in 80 fatal cases in which death seemed due to uncomplicated coronary lesions. They state that:

> Marching with a pack is considered as "vigorous exercise" and it is remarkable, in view of the soldier's chances for vigorous activity on or off duty, that about 40 per cent of these men had not had such exercise within a day or so of their final cardiac break.
>
> In 15 cases sudden death or the onset of severe pain in a fatal seizure occurred during vigorous or violent muscular effort. Twenty-six patients, or 35 per cent, had the fatal attack within one to several hours after "vigorous exercise."

Arteriosclerosis was the underlying pathologic basis of coronary occlusion in all cases.

Cardiac pain, particularly that of angina pectoris, is characterized by appearing during effort or emotional stress and by relief on rest. Appreciation of the importance of effort or excitement as a precipitating factor in angina pectoris or acute myocardial infarction should lead the physician to make direct inquiry regarding all attendant circumstances prior to the onset of the attack. Much significant information not spontaneously volunteered by the patient frequently will be uncovered. The appearance of distress on exertion or under emotional stress should indicate a tentative diagnosis of angina pectoris, of coronary failure or insufficiency, or of myocardial infarction[7] until such a diagnosis is clearly excluded on the basis of further evidence. In such a situation vigilance must be exercised for the signs or symptoms of myocardial infarction. In some instances, such as case 3, persistent weakness may be the sole finding, the significance of which may be corroborated only subsequently by progressive characteristic changes in later electrocardiographic tracings.

It is of interest that, aside from emotional stress and effort, other concomitant factors, such as exposure to cold or eating, which increase the work of the heart may superimpose their effect. Thus, in cases 7 and 11 exposure to cold by swimming and a cold shower may not have been entirely coincidental.

In the light of these considerations, medical officers should maintain close supervision over all those assigned to their care when they undertake strenuous or prolonged activities. The occurrence of substernal distress under these circumstances should cause the medical officer to advise cessation of such strenuous activity in order to forestall, when possible, the development of acute myocardial infarction. Even if myocardial infarction occurs, immediate enforcement of complete rest may be expected to influence the extent of the infarct and favor recovery. In any patient, previously well, who suddenly develops angina pectoris on rest or on exertion, one must suspect coronary narrowing or occlusion even if none of the signs of cardiac infarction appear.[7]

The several mechanisms which are operative in producing myocardial infarction are clarified by recent advances in our knowledge of the pathology of coronary arteriosclerosis and may be summarized as follows:

1. *Relative Ischemia.*—In previous studies that my associates and I have made on patients dying with acute myocardial infarction, no fresh thrombosis or occlusion was found by the injection plus dissection method of Schlesinger[8] in certain instances. It is logical to assume on the basis of actual pathologic findings and clinical experience that an artery narrowed by arteriosclerotic changes may transmit sufficient blood for the ordinary needs of the myocardium but may not be competent to transmit the increased blood flow required by the heart during effort. The heart muscle, under such circumstances, suffers from relative ischemia. If this is sufficiently prolonged, irreversible damage, i. e. infarction, results[9] (case 3). Sudden death may be due to the development of ventricular fibrillation or cardiac standstill because of myocardial ischemia in the absence of any fresh pathologic changes in the coronary arteries.

2. *Subintimal Hemorrhage.*—That coronary occlusion and coronary thrombosis frequently result from hemorrhages within the coronary arterial wall has been clearly demonstrated.[10] These pathologic studies offer an adequate basis for the sudden onset of symptoms of angina pectoris or of coronary occlusion. The formation of a hematoma within the wall of an artery may raise the intima and partially occlude the lumen. This early lesion was revealed in case 9, in which death occurred before there could be any further sequence of events. At times the hemorrhage may elevate the intima sufficiently to bring opposing surfaces together and completely occlude the lumen. In some instances the hemorrhage may rupture the intima, exposing a raw open hemorrhagic wound. This raw surface constitutes a favorable site for the development of a thrombus. Subintimal hemorrhage and subsequent thrombus formation may develop gradually over a period of many days or even a week or two and serve to explain some cases in which an appreciable interval separates the strenuous activity from the acute attack. It is not believed that subintimal hemorrhages occur in a normal artery but take place only in an atheromatous lesion.

The exact factors which determine hemorrhage from an intimal or subintimal capillary into the wall of an arteriosclerotic coronary artery have been the subject of speculation by various authors.[11] It has been suggested that intimal capillaries, since they arise directly from the lumen, are particularly susceptible to the transient increased coronary pressure induced by exertion or emotion. Intimal or subintimal capillaries are more liable to rupture if softening, which is a physical characteristic of atheromatous lesions, occurs and allows the pressure of blood within the capillary to dilate its walls to the extent that rupture is more prone to occur. The fragility of the capillary wall may also be affected

6. French, A. J., and Dock, W.: Fatal Coronary Arteriosclerosis in Young Soldiers, J. A. M. A. **124:** 1233 (April 29) 1944.

7. Blumgart, H. L.; Schlesinger, M. J., and Davis, D.: Studies on the Relation of the Clinical Manifestations of Angina Pectoris, Coronary Thrombosis and Myocardial Infarction to the Pathologic Findings, Am. Heart J. **19:** 1, 1940. Blumgart, Schlesinger and Zoll.[9]

8. Schlesinger, M. J.: An Injection Plus Dissection Study of Coronary Artery Occlusions and Anastomoses, Am. Heart J. **15:** 528, 1938.

9. Blumgart, H. L.: Schlesinger, M. J., and Zoll, P. M.: Angina Pectoris, Coronary Failure and Acute Myocardial Infarction, J. A. M. A. **116:** 91 (Jan 11) 1941.

10. Horn, H., and Finkelstein, L. E.: Arteriosclerosis of the Coronary Arteries and the Mechanism of Their Occlusion, Am. Heart J. **19:** 655, 1940 and the references cited in footnote 11.

11. Paterson, J. C.: Capillary Rupture with Intimal Hemorrhage as a Causative Factor in Coronary Thrombosis, Arch. Path. **25:** 474 (April) 1938. Wartman, W. B.: Occlusion of Coronary Arteries by Hemorrhage into Their Walls, Am. Heart J. **15:** 459, 1938. Winternitz, M. C.; Thomas, R. M., and LeCompte, P. M.: The Biology of Arteriosclerosis, Springfield, Ill., Charles C Thomas, Publisher, 1938. Blumenthal, B., and Reisinger, J. A.: Prodromal Pain in Coronary Occlusion, Am. Heart J. **20:** 141, 1940. Nelson, M. G.: Intimal Coronary Artery Hemorrhage as a Factor in the Causation of Coronary Occlusion, J. Path. & Bact. **53:** 105, 1941.

by anoxemia, by the presence of local or general toxic factors and by impaired nutrition. In addition, one may speculate as to whether the capillary wall may not share with neighboring tissues the anoxemia due to relative insufficiency of blood flow during effort or emotion and thus be more liable to rupture.

3. *Rupture of Atheromatous Abscess.*—Attacks of acute myocardial infarction following effort may also arise as the result of coronary occlusion following the rupture of an atheromatous abscess,[12] as in case 4.

Recognition of the causal relationship of effort to acute myocardial infarction should not lead the medical officer or physician to ascribe every attack of acute myocardial infarction to preceding effort. The occurrence of acute myocardial infarction in the foregoing cases during or immediately after strenuous effort clearly establishes a causal relationship. As with most diagnostic problems in medicine, the relation of effort to an attack of myocardial infarction in a particular patient may be certain, may be probable, suggestive or improbable or may be considered to be nonexistent. The relation is considered definite if the following criteria are satisfied.

1. The development and increase of cardiac symptoms such as pain or substernal distress during or immediately following unusual effort (cases 1-9, 11).
2. Continuation of the symptoms after cessation of effort.
3. The presence of the clinical signs and symptoms of acute myocardial infarction.
4. Development of the characteristic electrocardiographic pattern of acute anterior, posterior or lateral wall myocardial infarction.

If several days intervene between effort and development of acute myocardial infarction, the relation cannot be considered definite unless there is a continuity of symptoms bridging the interval.

The pathologic mechanisms that have been described offer a rational basis for those cases in which no symptoms are experienced for several days or a week or more following unusual effort. The sequence of pathologic events revealed by postmortem studies indicates that subintimal hemorrhages may lead to a gradual growth of the hematoma within the arterial wall or to the gradual formation of an intra-arterial thrombus over the site of the subintimal hemorrhage. Under such circumstances or when the thrombus propagates slowly, particularly when some prior collateral circulation has been developed, a symptomless interval of considerable duration between effort and myocardial infarction is understandable. The occurrence of such a succession of events in a patient with a symptomless interval should, however, be accepted with great caution and is to be considered probable, suggestive or improbable according to the nature of the effort, the length of the symptomless interval and the presence or absence of the other criteria mentioned.

In a patient in whom postmortem examination discloses arteriosclerotic obstruction or narrowing of the coronary artery but no fresh changes, the possibility of relative ischemia causing cardiac standstill or ventricular fibrillation must be entertained.

The evidence brought forward in this communication and by others demonstrates the importance of effort in precipitating attacks of acute myocardial infarction in a small but definite proportion of cases and supports the ischemic theory of cardiac pain. That emotion may likewise be the responsible precipitating factor is generally recognized and is further supported by objective evidence for the existence of reflex factors.[13] If inordinate myocardial strain is avoided in those suffering from angina pectoris, and if, in those suffering from acute myocardial infarction, the diagnosis is made early and appropriate treatment is instituted promptly, many catastrophes doubtless can be avoided. Clinical evidence, experimental observations and our knowledge of the collateral circulation within the heart conform to these considerations.[14]

12. Leary, T.: Pathology of Coronary Sclerosis, Am. Heart J. **10**: 328, 1935.

SUMMARY AND CONCLUSIONS

1. The histories of 11 patients with acute myocardial infarction consequent to strenuous effort illustrate the relationship between the two.

2. The clinical criteria which must be satisfied to demonstrate this relationship are (*a*) the development and increase of cardiac symptoms such as pain or substernal distress during or immediately following unusual effort, (*b*) continuation of the symptoms after cessation of effort, (*c*) presence of clinical signs and symptoms of acute myocardial infarction and (*d*) the development of characteristic electrocardiographic pattern of acute anterior, posterior or lateral wall myocardial infarction.

3. The pathologic mechanisms which induce acute myocardial infarction during or soon after effort are (*a*) subintimal hemorrhages or the rupture of an atheromatous abscess following strenuous effort and (*b*) the occurrence of relative ischemia brought about by strenuous effort and resulting in a need for increased blood flow which the arteriosclerotic vessels are unable to meet.

13. Freedberg, A. S.; Spiegl, E. D., and Riseman, J. E. F.: Effect of External Heat and Cold on Patients with Angina Pectoris: Evidence for the Existence of a Reflex Factor, Am. Heart J. **27**: 611, 1944.

14. Blumgart, H. L.: Cardiac Pain, Research Nerv. & Ment. Dis., Proc. (1942) **23**: 327, 1943.

From the Bureau of Laboratories, New York City Health Department.

The penicillin used in these studies was furnished by the Office of Scientific Research and Development from supplies assigned by the Committee on Medical Research for experimental investigations recommended by the Committee on Chemotherapeutics and Other Agents of the National Research Council.

PENICILLIN IN THE TREATMENT OF PNEUMOCOCCIC MENINGITIS

A STUDY OF 67 CONSECUTIVE CASES

EMANUEL APPELBAUM, M.D.
AND
JACK NELSON, M.D.
NEW YORK

During a period of nearly thirty-five years the members of the Division of Acute Infections of the Central Nervous System of the New York City Health Department have been studying the effect of the various forms of therapy in bacterial meningitis. Before the newer chemicals became available the case fatality in pneumococcic meningitis was 100 per cent.

The use of azosulfamide and sulfanilamide slightly improved the prognosis. The advent of the more potent sulfonamides marked a further advance in the treatment of this disease. In an unpublished series of 139 cases of pneumococcic meningitis treated with sulfapyridine, sulfadiazine, sulfathiazole or a combination of these (and specific serum when available) we obtained 49 recoveries. The recent introduction of penicillin led us to try the use of this drug in pneumococcic meningitis.

MATERIAL

This report is based on a series of 67 consecutive cases seen between Oct. 10, 1943 and May 1, 1944. The diagnosis was definitely established in each instance by culturing and typing the organisms from the spinal fluid.

TABLE 1.—*Age Distribution in 67 Cases of Pneumococcic Meningitis*

Number of Recoveries in Each Group

Age Years	Number of Cases	Number of Recoveries
Under 1	11	4
1 to 10	6	5
11 to 20	2	1
21 to 30	1	1
31 to 40	7	4
41 to 50	12	3
51 to 60	14	5
61 to 70	10	1
71 to 80	4	2
Totals	67	26

CLINICAL ASPECTS

Table 1 shows the age distribution of the patients in this series. The wide range in age is quite evident. It is also of interest to note that the number of patients under 1 year together with those above 50 years of age constitute more than half of the total number of cases. Most of the patients presented the typical picture of meningitis on admission. The individual patients showed considerable variation in the severity of the disease, but most of them appeared critically ill and 12 even moribund.

Consideration of the foci of infection is of the utmost importance. As shown in table 2, a definite focus in the ear or mastoid or both was found in 30 of these 67 cases. In 1 of the cases with otitis and mastoiditis there was also a petrositis. While this series shows a record of only 2 instances of definite sinus involvement, it is possible that this condition existed more frequently than it was recognized. In 1 instance there was a fractured skull and in 1 a head injury with a possible fracture. In 17 patients the presence of pneumonia was regarded as the probable primary focus. In 2 of these there was a complicating empyema and in 1 instance a vegetative endocarditis. There remained 16 cases in which the meningitis was preceded either by no obvious illness or by a simple upper respiratory infection. It is highly probable also that in not a few of the cases there were multiple foci of infection.

TABLE 2.—*Primary Foci of Infection*

Number of Recoveries in Each Group

Type of Focus	Number of Cases	Number Recovered
No known focus *	16	4
Otitis media with or without mastoiditis	30	15
Pneumonia	17	5
Sinusitis	2	0
Head injury	2	2
Total	67	26

* In this group were also included cases of simple respiratory infections.

BACTERIOLOGIC DIAGNOSIS

Diagnostic lumbar punctures were performed in all of the cases on admission. The cerebrospinal fluid showed varying degrees of turbidity. The cells were greatly increased in number with polymorphonuclears predominating. In the majority of instances the protein content was moderately to greatly increased. Sugar was either absent or considerably diminished in almost all instances. The diagnosis was confirmed bacteriologically in all cases. Stained smears of the cerebrospinal fluid showed varying numbers of gram positive diplococci in 63 instances. Pneumococci were grown from the fluid in all of the 67 cases. The organisms were typed in all the cases from the cultures and in many instances directly from the spinal fluid. The distribution of these types is shown in table 3. It may be of interest to note that when type III was recovered the meningitis was almost always secondary to otitis media, mastoiditis or sinusitis. Blood cultures were made in 49 of the cases prior to the institution of sulfonamide or penicillin therapy. These were positive in 33 instances.

TREATMENT

All the patients in this series were treated with penicillin. In all but 1 instance sulfonamides were used prior to the institution of penicillin therapy. Sulfathiazole alone was used in 1 case. In the remaining 65 cases sulfadiazine was employed either alone or combined with sulfathiazole. The total amount of sulfonamide given before penicillin was begun varied from 1.5 to 97 Gm., with an average of 22 Gm. The organisms isolated from the spinal fluid in every case were tested for sulfonamide sensitivity. In only 1 of these was there evidence of sulfonamide fastness. In 4 instances there was already evidence of a satisfactory clinical response to sulfonamide as well as a sterile spinal fluid at the time penicillin therapy was instituted.

TABLE 3.—*The Types of Pneumococci*

	Type of Pneumococcus																					
Primary Focus	1	2	3	4	5	6	7	8	12	14	18	19	21	22	23	28	33	34	36	40
Otitis, mastoiditis, sinusitis	3	..	10	2	3	1	1	1	..	3	..	2	..	..	2	..	1	..	1	1
Pneumonia	..	..	..	2	1	..	2	2	5	..	..	..	1	1	..	1	..	1	..	..
Head injury	..	..	1*	..	..	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..
Unknown	1	1	..	..	2	1	..	2	6	1	2	2	..	..	..	..	..	..	..	..
Total	4	1	11	4	6	2	4	5	11	4	2	4	1	1	2	1	1	1	1	1

* = Fracture through mastoid.

TABLE 4.—*Duration of Illness Before Institution of Penicillin Therapy*

Number of Days	Number of Cases	Number of Days	Number of Cases
1	4	9	0
2	16	10	2
3	11	11	0
4	10	12	0
5	5	13	0
6	4	14	1
7	3	21	1
8	2	Unknown	8
Total			67 cases

Rammelkamp and Keefer [1] have demonstrated that penicillin administered intravenously or intramuscularly does not pass through the meningovascular barrier in significant quantities. Injected intrathecally,[2]

1. Rammelkamp, C. H., and Keefer, C. S.: The Absorption, Excretion and Distribution of Penicillin, J. Clin. Investigation **22**: 425 (May) 1943.

2. Rammelkamp, C. H., and Keefer, C. S.: The Absorption, Excretion and Toxicity of Penicillin Administered by Intrathecal Injection, Am. J. M. Sc. **205**: 342 (March) 1943.

penicillin is slowly absorbed from the subarachnoid space and may be detected in the spinal fluid thirty-one and one-half hours later. In subjects with meningitis absorption of penicillin after intrathecal injection was more rapid than in normals, but significant amounts of the antibiotic agent remained in the spinal fluid for a period of twenty-four hours. It was also demonstrated that lumbar injections resulted in a diffusion of the penicillin throughout the ventriculo-subarachnoid space. In the treatment of meningitis therefore it seemed necessary to use penicillin intrathecally as well as intravenously or intramuscularly.

All the patients in this series received penicillin intraspinally following the removal of an equal or somewhat larger amount of spinal fluid. Sodium penicillin was dissolved in isotonic solution of sodium chloride in a dilution of 1,000 units per cubic centimeter. The intrathecal dosage varied from 5,000 to 20,000 units and was administered at twelve or twenty-four hour intervals. In a few instances the drug was also administered intracisternally or intraventricularly and, in 2 cases, subdurally. The intrathecal administration of penicillin was as a rule continued for a varying number of days after clinical improvement was manifest and the spinal fluid no longer showed organisms or diminution in the sugar content. This precaution was necessary because of the frequency of relapses in this

TABLE 5.—*Initial Response to Penicillin and Ultimate Outcome of Case*

Type of Response	Number of Cases	Recovery	Death
Good	28	21	7
Fair	11	5	6
None	28	0	28
Total	67	26	41

form of meningitis. The total intraspinal dosage varied from 10,000 to 700,000 units, with an average of 175,000 units. It may be noted that in 3 instances the intraspinal route of administration alone was used.

Penicillin was also administered intramuscularly in most of the cases and in 11 instances it was administered intravenously by the continuous drip method. There were only 2 patients who did not receive penicillin either intramuscularly or intravenously. For the intramuscular administration the drug was prepared in a dilution of 5,000 units per cubic centimeter of saline solution and administered in doses of 2,500 to 10,000 units every three to four hours. When the drug was used intravenously we employed the continuous slow drip method at the rate of 2,500 to 5,000 units per hour. The total amount of penicillin administered intramuscularly or intravenously varied from 20,000 to 1,840,000 units, with an average of 400,000 units. It may be of interest to note that in 2 instances following mastoidectomy the operative wound was irrigated from three to four times a day with a solution of penicillin in a dilution of 1 to 1,000 units per cubic centimeter. This was repeated for four and nine days respectively.

In all but 13 instances sulfonamides were discontinued at the time penicillin therapy was instituted. Four patients received also antipneumococcus serum intravenously or intramuscularly or by both routes. A mastoidectomy, unilateral or bilateral, was performed in 14 instances. Other nonspecific measures of therapy included the use of insulin for 2 diabetic patients and the not infrequent administration of transfusions in many instances.

RESULTS

In this series of 67 cases there were 26 recoveries and 41 deaths, a recovery rate of 39 per cent. It will be seen from table 1 that the mortality was higher in the extremes of life, which include infants under 1 year and adults over 50 years of age. There also appeared to be a relationship between the primary focus of infection and the mortality, as shown in table 2. Perhaps the most definite correlation existed between bacteremia and the outcome. Among 33 patients with a positive initial blood culture there were 10 recoveries, while among 16 patients with negative blood cultures there were also 10 recoveries. On the other hand there was no evidence of a correlation between the duration of illness prior to the institution of penicillin therapy and the penicillin therapy and the outcome.

As shown in table 5, an initial favorable response was noted in 28 instances. In 21 of these, improvement progressed satisfactorily terminating in recovery, and in 7 cases the improvement was only temporary, resulting finally in a fatal issue. There were 28 patients who at no time showed any evidence of a clinical response and who died. It should be noted that among those who died there were 8 patients who were treated for less than twenty-four hours and received a total of less than 80,000 units of penicillin. The fatal group included also 1 instance of severe congestive heart failure, 2 cases of diabetes mellitus and 1 instance of severe sulfonamide intoxication. It is probable that these associated conditions were factors contributory to death. In 2 instances the development of brain abscess either early or late in the course of the disease undoubtedly contributed to the death of the patients. There was 1 patient with meningitis, pneumonia and endocarditis who at the time of her death showed no evidence of meningeal involvement. This was confirmed by the necropsy findings.

As previously noted, sulfadiazine was continued in the treatment of 13 of the patients after penicillin was instituted. Of these, 5 recovered and 8 died.

SPINAL FLUID CHANGES DURING THE COURSE OF TREATMENT

We have already referred to 4 instances in which the spinal fluids were sterile at the time of institution of penicillin therapy. In the remaining 65 cases, organisms were found in the spinal fluid prior to the use of this drug. With the institution of penicillin therapy fairly prompt disappearance of the pneumococci was noted in a vast majority of the cases. For example, the spinal fluid culture became sterile within forty-eight hours in 53 cases, and a negative smear was obtained within seventy-two hours in 36 instances. However, it should be emphasized that the early disappearance of the organisms could not be relied on as an index of the control of the infection.

With regard to the spinal fluid sugar, a return of this substance to normal within five days was observed in 31 patients. It is important to note that 20 of these recovered. It would seem therefore that an early return of the sugar to normal may be regarded as a favorable prognostic factor. It is necessary to caution against misinterpreting as normal the rise in the spinal fluid sugar resulting from intravenous glucose infusions.

In this connection it may be noted that penicillinase was not used in the cultures of this series. The effect of this enzyme on spinal fluid cultures is at present under investigation in our laboratory.

Penicillin determinations were made on each specimen of spinal fluid withdrawn. In 48 instances the spinal fluid organisms were studied for sensitivity to penicillin. These details will not be discussed at present but will form the subject of another report.

As mentioned previously, positive blood cultures were obtained in 33 cases before the initial sulfonamide therapy. Following penicillin therapy a blood culture was available in only 15 of these patients, in 13 of whom it became sterile.

It is well known that pneumococcic meningitis at times shows a tendency to relapse. In our series there were 7 instances with one or more relapses. In these cases there was evidence, both clinical and laboratory, of control of the infection for periods varying from three to thirty days before the disease recurred. Four of the patients with relapses recovered and 3 died.

COMPLICATIONS

In 2 instances the meningitis was complicated by brain abscess. These terminated fatally. The presence of subarachnoid block was noted in 6 cases. It is possible that the intrathecal penicillin therapy contributed toward the development of the complication. In 1 instance a meningeal infection due to Bacillus prodigiosus was superimposed in the terminal phase of the patient's illness.

REACTIONS

In 3 instances there were local tissue reactions at the site of the penicillin injection. These cleared up fairly rapidly. There were no other untoward effects following penicillin therapy in this series of 67 cases.

COMMENT

It is clear from this study that the introduction of penicillin has as yet not solved the problem of the treatment of pneumococcic meningitis. While this antibiotic agent was highly effective in the treatment of an appreciable number of cases, it proved ineffective in the majority of instances. However, there is no doubt that the use of penicillin resulted in the recovery of some patients who had failed to respond to sulfonamide.

Several factors contribute to the difficulty in successfully treating pneumococcic meningitis. The most important of these in our opinion is the fact that the meningitis is usually secondary to one or more primary foci of infection, many of which cannot be completely eradicated. We are at variance with a recent report,[3] based on a small series of cases, which minimizes the importance of the removal of suppurative foci. In our experience the complete eradication of the primary foci of infection is of the utmost importance in the management of this form of meningitis. Of course, a patient may recover without an operation. On the other hand, we have had 7 cases in which a mastoidectomy resulted in striking improvement after there had been failure to respond to penicillin therapy. In this connection we wish to stress that not infrequently a severe mastoiditis may fail to present clinical symptoms and occasionally even radiographic evidence of involvement.

Among other factors which militate against the success of therapy is the frequent presence of bacteremia. For instance, in this series of 33 patients with positive blood cultures 23 died, and among 16 cases with negative blood cultures there were only 6 deaths. Sometimes the infection is so overwhelming that the patient succumbs before adequate therapy can be administered. Furthermore, there is much that is unknown in regard to the bacteriology of the organisms, particularly with respect to the virulence of the various strains.

The precise method of treatment must at present be regarded as tentative. A number of important problems in connection with the employment of penicillin still remain to be investigated. These include an evaluation of the use of massive doses of the drug and the treatment of the disease with a combination of penicillin and sulfonamide.

SUMMARY

1. Sixty-seven consecutive patients with pneumococcic meningitis were treated with penicillin intrathecally and also intravenously or intramuscularly. In all but 1 instance, sulfonamides were used prior to the institution of penicillin therapy.

2. Of these 67 patients, 26 recovered and 41 died, representing a recovery rate of 39 per cent.

3. Thirteen of the patients were treated with a combination of penicillin and sulfadiazine. Of these, 5 recovered and 8 died.

4. The factors contributing to the difficulty of successfully treating pneumococcic meningitis include the presence of primary foci of infection, which are frequently inaccessible, the presence of bacteremia in many instances, and the occasional appearance of the disease in a fulminating form.

5. While penicillin was highly effective in the treatment of an appreciable number of cases, it proved ineffective in the majority of instances. It is evident that further investigation is needed to solve the problem of the treatment of pneumococcic meningitis.

3. Waring, A. J., Jr., and Smith, M. H. D.: Combined Penicillin and Sulfonamide Therapy in the Treatment of Pneumococcic Meningitis, J. A. M. A. **126**: 418 (Oct. 14) 1944.

Blaise Pascal (1623-1662).—The "great moralist," Blaise Pascal, was also a great scientist. His "Thoughts" ("Pensées") and "Letters"—in which he said "Pardon the length of this letter; I have not time to write you a short one"—are gems of French literature. Yet the sincere Jansenist turned to the dice game and the trials of the gaming table to develop, after Cardan, an unscrupulous Italian mathematician, and with Fermat, a cryptic French attorney, the mathematical theory of probability on which much of modern scientific thinking rests. Current weather forecasting and present day meteorology, on which the fortunes of aerial warfare depend, could hardly have been born until some one had established what Pascal—with the help of his brother-in-law, F. Perier—proved in the "Great Experiment" on the Puy de Dome; namely, the weight of the mass of the air. Here quoted is "the story of the great experiment," published posthumously in 1663. Employing Torricelli's recently invented barometer, Pascal slew forever the myth that "nature abhors a vacuum." Pascal was a child prodigy; before he was 11 he had taught himself geometry, drawing figures with charcoal on the tiles of his playroom and giving his own names to the lines and curves which his doting father had forbidden him to study. A great mathematician, inventor of the adding (calculating) machine and the hydraulic press, Pascal has been honored by having a law (of fluid pressure), a triangle and a mystic hexagram named after him.—The Autobiography of Science, edited by Forest Ray Moulton and Justus J. Schifferes, New York, Doubleday, Doran & Co., Inc., 1945.

THE METHYLENE BLUE TEST IN INFECTIOUS (EPIDEMIC) HEPATITIS

CAPTAIN SYDNEY S. GELLIS
MEDICAL CORPS, ARMY OF THE UNITED STATES
AND
JOSEPH STOKES JR., M.D.
PHILADELPHIA

The methylene blue test described by Franke [1] as a method for the detection of bilirubin in urine was used by Stokes and Neefe [2] in an outbreak of infectious (epidemic) hepatitis with results which indicated its possible value in the early diagnosis of the disease. In further investigating a modified methylene blue test suggested by Franke and first employed by Fellinger and Menkes,[3] Neefe [4] found the modified test to be of value in determining the presence of biliary pigments in the urine in the preicteric stage of the disease and occasionally before a significant increase in the concentration of total serum bilirubin was found. Because of its simplicity the modified test, although somewhat less sensitive than the Harrison spot test, was employed during the course of an investigation of infectious (epidemic) hepatitis in the Mediterranean theater of operations from November 1944 to February 1945. The present report is confined to data obtained in the study of the preicteric, icteric and posticteric stages of cases of infectious hepatitis with jaundice.

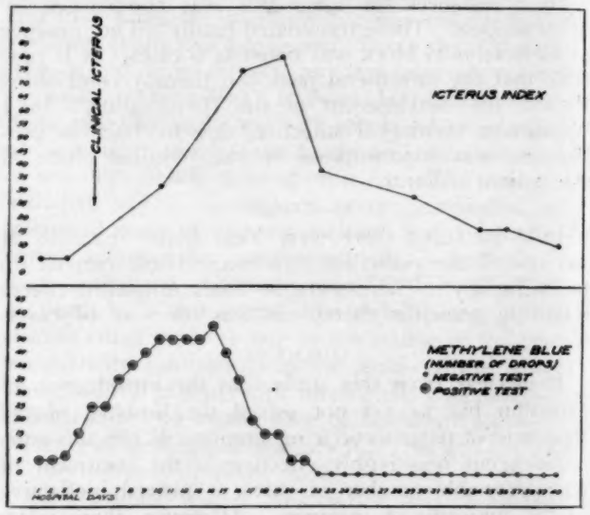
The modified methylene blue test was performed as follows: To 5 cc. of a prebreakfast urine specimen were added 2 drops of an 0.2 per cent aqueous solution of methylene blue chloride. If a green color resulted, more methylene blue was added dropwise and the last drop required to convert the green color to blue was recorded. Pipets were used which delivered 20 drops of the solution per cubic centimeter. Methylene blue chloride proved to be satisfactory in that the dye content of different lots showed little variation. When readings were made by natural light, no difficulty was found in determining the change from a green color to blue. If more than 5 drops were required to produce the color change, the urine was diluted with distilled water and methylene blue was again added drop by drop until the end point was reached. Correction was then made for the dilution factor. This was found to be necessary because the addition of more than 5 drops of methylene blue resulted in a color of such intensity that the end point was difficult to determine.

Methylene blue tests on the prebreakfast urine specimens of 1,000 patients with diseases other than hepatitis gave the following results: Seventy-four per cent of the urine specimens yielded a blue solution after the addition of 2 drops of the reagent, 24.3 per cent required 3 drops and 1.7 per cent required 4 drops in order to convert the resulting green color to blue. Thus in this series of 1,000 patients no urine specimens yielded a green reaction after the addition of 4 drops of the reagent. On the basis of the foregoing results a test of 5 drops or more was considered positive.

Daily methylene blue tests were performed on the morning urine specimens of 77 patients with hepatitis with jaundice. Of the 77, 44 were jaundiced at the time of admission to the hospital and 33 developed jaundice subsequent to the date of admission. The methylene blue test became positive in the 33 patients with preicteric hepatitis one to six days before scleral icterus made its appearance. The exact number of days during which the methylene blue test was positive prior to the appearance of scleral icterus is shown for each case in the accompanying table.

At the time when the methylene blue test first became positive, 12 of the 33 patients had normal icterus indexes while the remaining 21 patients had icterus indexes which were either at the upper limits of normal or were slightly elevated.

Thus from the foregoing data it was possible to suspect hepatitis in 33 patients one to six days before clinical icterus became apparent and in 12 of the 33 patients before the icterus index was elevated.



Methylene blue tests during the preicteric, icteric and posticteric stages.

The methylene blue test also proved to be of value in following the course of these patients, in that titration of serial dilutions of the urines served as a rough approximation of the icterus index. However, after the height of jaundice had been reached and the patients' convalescence had begun, the methylene blue test became negative although clinical icterus was present and the icterus index was still elevated. The range of the icterus index in which the test became negative for the 77 patients studied was between 35 and 20 despite the fact that during the preicteric and early icteric stages the test was positive in the presence of a normal or slightly elevated icterus index. To illustrate these findings, the accompanying chart records the methylene blue tests during the preicteric, icteric and posticteric stages of 1 of the patients in the series.

Studies of urobilinogen excretion in these patients were conducted by Major Phillip Hallock and will be reported elsewhere. The results coincided with the findings of the methyelene blue test, but the chief advantage of the latter test lay in its simplicity and

From the Department of Pediatrics, University of Pennsylvania School of Medicine.

Lieutenant Colonel Robert Hebbel and his staff at the 26th General Hospital gave assistance.
This work was carried out under the direction of the Commission on Measles and Mumps of the Army Epidemiological Board, Preventive Medicine Service, Office of the Surgeon General, U. S. Army.

1. Franke, K.: Methylenblau, ein einfaches sehr empfindliches Reagens zum Nachweis von Bilirubin, Med. Klin. **27**: 94, 1931.
2. Stokes, J., Jr., and Neefe, J. R.: The Prevention and Attenuation of Infectious Hepatitis by Gamma Globulin, J. A. M. A. **127**: 144 (Jan. 20) 1945.
3. Fellinger, K., and Menkes, K.: Quantitative Bilirubin Determination in the Urine with the Methylene Blue Method, Wien. klin. Wchnschr. **46**: 133 (Feb. 3) 1933.
4. Neefe, J. R.: Personal communication to the authors.

the ease with which a large number of determinations could be made.

Of the 77 patients studied, 5 developed relapses characterized by the development of fever, abdominal pain, nausea, vomiting and enlargement and tenderness of the liver. In all 5 the cephalin cholesterol flocculation test which had previously returned to normal became strongly positive again and the methylene blue test likewise became positive. Four of the patients developed no rise in icterus index during the relapse, while the fifth patient became jaundiced for the second time. Thus the methylene blue test in these cases also served to warn of an impending relapse.

COMMENT

In February 1945, when the present studies had been completed, a report on the use of the methylene blue test in patients with liver damage due to tetrachlorethane was published by Myers.[5] In that study the test was performed by adding 2 drops of Loeffler's methylene blue to 10 cc. of urine. If a green color resulted, the test was considered positive; the test was repeated with increasing dilutions of the urine until the dilution was reached in which 2 drops of the reagent produced a blue color. Myers' findings in tetrachlorethane poisoning are similar to our results in infectious hepatitis in that the methylene blue test became positive prior to an elevation of serum bilirubin and subsequently became negative before the return of serum bilirubin to normal limits. Thus in liver damage due to tetrachlorethane the methylene blue test permitted the prediction of impending icterus, facilitating the prompt removal of the patient from further exposure to the toxic fumes.

Cases Showing Positive Methylene Blue Tests Prior to Jaundice

Number of hospital days preceding clinical jaundice	1	2	3	4	5	6
Number of cases showing positive methylene blue tests	7	10	5	6	4	1

The exact mechanism of the methylene blue test is uncertain. Myers feels that the green color resulting from the addition of methylene blue to bilirubin is due primarily to a mixture of pigments. According to Reinhold,[6] chemical reaction occurs between methylene blue and bilirubin but his studies also indicate that the contribution of this reaction to the development of the green color is less important than is the effect of blending the blue with the yellow bile pigment. There appears to be no explanation at present to account for a negative methylene blue test during the convalescent stage of hepatitis when serum bilirubin is still elevated, whereas the test is strongly positive in the preicteric stage although serum bilirubin may be normal at the time. If the methylene blue test is a measure of bilirubin in the urine, a variation in renal threshold resulting perhaps from alteration in the availability of the bilirubin for renal excretion, or a chemical alteration of bilirubin may account for the foregoing findings. Further investigation will be necessary to clarify these points.

5. Myers, C. P.: Use of Methylene Blue in Testing for Bilirubin in the Urine, J. Indust. Hyg. & Toxicol. **27**: 52, 1945.
6. Reinhold, J. G.: Personal communication to the authors.

SUMMARY

The modified methylene blue test for bilirubin in the urine employed in a study of infectious (epidemic) hepatitis with jaundice proved of value (*a*) in the early diagnosis of preicteric hepatitis, (*b*) in evaluating the course of the disease and (*c*) in the prediction of impending relapse. Because of the simplicity of the test, it appears most useful in large scale testing during the course of an outbreak of infectious hepatitis and in installations where complete laboratory facilities are lacking.

GAS GANGRENE

A STUDY OF 96 CASES TREATED IN AN EVACUATION HOSPITAL

LIEUTENANT COLONEL FRANCIS H. LANGLEY
Chief of Surgical Service
AND
CAPTAIN LAWRENCE B. WINKELSTEIN
MEDICAL CORPS, ARMY OF THE UNITED STATES

The high incidence of gas gangrene infection in modern warfare and the difficulties encountered in the treatment and cure of the disease have been and still constitute a major medical problem. It has been estimated that the incidence of gas gangrene in the African campaigns of 1942 and 1943 was as high as that encountered in France during the world war of 1914-1918. Although these anaerobic infections were not especially common in the Tunisian campaign (2 to 7 cases per thousand wounded) they were definitely more prevalent in Sicily (10 cases per thousand wounded) and were considered to have been the most troublesome infection encountered in forward military areas during the Italian campaign of 1943-1944 (20 cases per thousand). These figures acquire additional importance when MacLennan and MacFarlane[1] estimate that the case fatality of gas gangrene in the present war has been approximately 50 per cent.

Statistical data are not yet available on the incidence of the disease among those wounded in France. It is known, however, that during the period of September 1943 to and including December 1943 the incidence among the American troops in Italy approximated 6 cases per thousand battle casualties.

The problem of the diagnosis and treatment of gas gangrene is one peculiar to the level of medical care of the evacuation hospital. It is at this level that the disease is first encountered and also at this level that definitive treatment must be devised and executed. Since the operational activation of this evacuation hospital in France we have had the opportunity of studying and treating a larger number of cases of gas gangrene than would normally be seen in a medical unit of this type. The total number of cases of anaerobic gas producing infections treated at the eight different installations of this hospital from July 25 to Dec. 1, 1944 has been 96, which signifies a gross incidence of 9.5 cases per thousand admissions, or a corrected incidence of 16.0 per thousand surgical cases. This figure, although high, does not quite reach the proportions

The entire hospital unit cooperated in this work. Capt. R. E. Hultkrans, M. C., and Capt. E. N. Bookrajian, M. C., of the Surgical Service performed many of the operative procedures. Second Lieutenants Edna May Rutherford, A. N. C., and Angelina Russo, A. N. C., helped in compiling the statistics and gave untiring devotion in the care of the patients.

1. MacLennon, J. D., and MacFarlane, M. G.: Brit. M. J. **1**: 683 (May 20) 1944.

(20 per thousand battle casualties) found in the early weeks of the Italian campaign in the British Eighth Army.

Because of this relatively large number, an attempt was made to determine what errors of omission or commission had been made and, if possible, to see what further measures could be taken both to reduce the incidence and to improve the treatment. With this in mind, various studies of our cases, individually and collectively, were made.

STATISTICAL STUDY OF GAS GANGRENE

1. *Incidence.*—In preparation for these studies a statistical review of all cases of gas gangrene diagnosed and treated at the various installations of this hospital in northern France was made. Only such cases as could be positively diagnosed as gas bacillus infections are included, and all questionable or doubtful cases are excluded from the series here reported. These cases, tabulated against the total number of surgical cases treated, are expressed in table 1, a study of which reveals the obviously high incidence of gas gangrene infection among the prisoners of war. These prisoners included not only Germans but also Czechs, Rumanians, Bulgars, Poles, Austrians and some Russians. With this group the incidence per thousand surgical casualties was 51.9, which is over six times the American

TABLE 1.—*Incidence of Gas Gangrene*

	Total	United States	Prisoners of War	Free French	Civilians
Surgical casualties	6,000	4,051	1,040	652	257
Cases of gas gangrene	96	32	54	8	2
Per cent of total cases of gas gangrene	100	33.3	56.3	8.3	2.1
Incidence per thousand surgical cases	16.0	8.0	51.9	12.3	7.8

incidence of 8.0, or four times that of the Free French, which was 12.3. Attempts at explanation of this will be made later. It has been our duty on two occasions to care for many such German wounded, the majority of whom, before their admission, had had no previous therapy other than the simplest of first aid measures. In 1 instance over 380 such prisoners, with all types of wounds, were brought at one time into the hospital, already nearly filled to capacity. These prisoners were taken from a nearby German sanatorium where neither doctors nor medical equipment were available. There resulted a tremendous backlog for surgery, and many of these wounded had to remain for several days before they reached the surgical tents. At the same time our incidence of gas gangrene reached its peak, with 22 confirmed cases within a period of three days. At another installation the relationship of German casualties, as compared with those of the combined American and French injured, was 2 to 1. At this time 386 surgical cases were completed in a period of less than four days. The incidence of gas gangrene at this time was 11 cases among the prisoners of war, 1 case in a French soldier and none among the American wounded.

2. *Criteria for the Diagnosis of Gas Gangrene.*—Many patients admitted to the hospital were already patently infected with gas gangrene at the time of admission. As our series of cases grew, we were able to establish various criteria for diagnosis so that these potentially dangerous cases could get surgical priority. The criteria for a tentative diagnosis of gas gangrene at admission or preoperatively was as follows:

1. History of:
   (a) Pain, especially with a feeling of tension, heaviness or tightness of the dressing. This was the most frequent and the most striking complaint and was present in almost 100 per cent of the cases in which an early diagnosis was made.
   (b) A clinical degree of toxemia, often coupled with definite mental changes. This was noticed in about 75 per cent of the cases admitted and varied greatly in degree and depth.
   (c) In more advanced cases a typical change in general skin color. This varied from an extreme pallor with a bluish brown tinge to a semibronzing not only of the skin around the wound but also of the face, the lips and the body in general.
2. A high pulse rate, usually over 110 and frequently above 120, out of proportion to either the degree of infection present or the degree of toxemia.
3. Elevation of temperature. A majority of those wounded in battle admitted to the hospital had normal or subnormal temperatures as a result of the inhibitory effect of early sulfonamide therapy. In all of the suspected gas gangrene cases the temperature was elevated regardless of sulfonamides, usually from 100 to 102 F. Here also the elevation of temperature was much higher than would be suggested by the degree of infection or toxemia.
4. Anemia, with a tendency to increase in severity. This usually was out of proportion to the amount of hemorrhage but in definite relationship to the length and severity of the toxemia.
5. The wound:
   (a) An odor, best described as "rotten or decaying meat" or "mousey," and entirely different from the odor of other gross infections or contaminations. This typical odor was present in only about a third of the cases which were diagnosed on admission. In the remainder it was either absent or was masked by the odor of Escherichia coli or other putrefactive organisms.
   (b) In early cases no remarkable change around the area of the wound. The crepitus, so often described was noted in only a few cases. Similarly the textbook description of the mottling or bronzing of the skin at the edges of the wound was not noted frequently. A few cases of subcutaneous, well demarcated edema were seen.

Tentative diagnosis was not made on any one single finding but rather on the correlation of several findings. With each such tentative diagnosis every attempt was made to get the patient in the best possible physical condition for surgery at the earliest possible moment, where the diagnosis was either corroborated or disproved.

It must be understood that under conditions such as are found in an evacuation hospital, and with only limited laboratory facilities available, the absolute diagnosis of clostridial infection is impossible. For similar reasons it has been impossible to classify the various types of anaerobes which are virulent gas formers. Final diagnosis was made by the gross appearance of the wound at surgery (at least two surgeons concurring) together with the clinical preoperative and postoperative course and laboratory findings. The criteria for diagnosis before and at surgery, and for determination of further therapy, consisted of:

1. Clinical course of the patient between admission and operation: Increases in pulse rate, temperature and degree of toxicity, with special emphasis on the last mentioned.

2. X-ray findings: X-ray facilities were of the best, and it was not infrequently that the radiologist reported gas shadows along muscle planes, other than shadows of imprisoned air, in his routine radiographic reports. X-ray evidence of gas was never used, however, for other than supportive information.

3. Microscopic examination of muscle smear: Thorough, careful and precise studies of muscle and exudate smears, stained by the Gram method, were made in every case. The pathologist examining these smears exercised most conservative judgment in pronouncing them to be positive. All doubtful specimens were considered negative. No case with "negative" smears, regardless of other findings, was considered to be gas gangrene.

4. Appearance of the wound at operation: Characteristic color changes and crepitation were not often found. What was noted frequently in all positive cases was a typical subcutaneous edema, which was present around the site of the lesion and which spread outward from that area in a rather well demarcated zone. Gas bubbles were found often but alone were not considered diagnostic unless they were more than localized and were present in the muscle planes. The most characteristic finding, however, was the typical picture of the muscle tissue itself. The muscles seemed to be affected individually and characterized by death of the tissue, an edematous appearance and color changes varying from a deep dirty brown through a green to a gray.

3. *Time of Diagnosis.*—Accordingly, with the foregoing classification as a basis, the diagnosis of gas gangrene was made at one of three stages in the clinical course of the patient: (1) on admission or soon after, (2) at the time of operation and (3) postoperatively. The result of this classification is expressed in table 2.

Thus, briefly, we were able to diagnose tentatively one third of all our cases of gas gangrene either at the time of admission to the hospital or shortly thereafter. With increasing experience, more and more cases are being thus classified. All these were later confirmed at operation. Similar tentative diagnoses were made in approximately 15 other cases, which, however, were later disproved. Of the total number 57.4 per cent were diagnosed for the first time at operation. Seven cases, or 7.3 per cent of the total number, either were misdiagnosed when the original débridement was done or the infection developed in these cases subsequent to surgery.

4. *Age and Sex Incidence.*—All cases reported here are in males. The youngest, aged 17, and the oldest, aged 44, were both prisoners of war. The average age for the entire group was 26.2 years. All patients were apparently in good physical condition at the time the injuries were received, nor was there any evidence of long standing malnutrition, avitaminosis or systemic disease present even in the captured Germans.

TABLE 2.—*Time of Diagnosis of Gas Gangrene*

	United States	Prisoners of War	Free French	Civilians	Total	Per Cent of Cases
Gas infection diagnosed as presumably present when first seen	6	27	1	..	34	35.4
Gas infection diagnosed at operation (not including the preceding, which were confirmed at this time)	20	26	7	2	55	57.4
Gas infection developing postoperatively	6	1	..	..	7	7.2
Total	32	54	8	2	96	100.0

5. *Agents.*—All infections included in this series in which gas gangrene developed, save 1, were the results of battle casualties. Of the total of 96 cases 48 cases, or 50 per cent, were the direct result of mortar or other high explosive shells; 17 cases, or 17.7 per cent, occurred subsequent to mine detonations; 10 cases, or 11 per cent, were due to booby trap explosions, and the remainder were due to gunshot wounds. The 1 case which was not a battle casualty occurred in a French civilian who received his injuries as the result of a fall from a fast moving motorcycle.

TABLE 3.—*Time Between Wounding and Therapy in 73 of 96 Cases*

	United States	Prisoners of War	Free French	Total
Wound to first dressing:				
Immediately	12	6	1	19
Up to 1 hour after injury	10	8	4	22
1 - 6 hours after injury	4	13	..	17
6 -12 hours after injury	..	8	..	8
12 -24 hours after injury	..	5	..	5
Over 24 hours after injury	..	2	..	2
Average time wound to initial dressing	12 min.	5 hrs. 40 min.	18 min.	
Wound to admission to hospital:				
1 - 2 hours after injury	1	..	..	1
2 - 6 hours after injury	12	1	..	13
6 -12 hours after injury	14	3	1	18
12 -24 hours after injury	1	14	3	18
1 - 2 days after injury	2	11	..	13
2 - 3 days after injury	..	7	..	7
3 - 4 days after injury	..	3	..	3
Average time wound to admission in hospital	14.7 hrs.	42.6 hrs.	15 hrs.	
Wound to operation:				
6 - 12 hours after injury	1	..	..	1
12 - 24 hours after injury	18	1	1	20
24 hours to 2 days after injury	8	8	2	18
2 - 3 days after injury	..	6	1	7
3 - 4 days after injury	1	2	..	3
4 - 5 days after injury	1	12	..	13
Over 5 days after injury	..	11	..	11
Average time to operation	1 day	3¾ days	1½ days	
Incidence per thousand battle casualties	8 per 1,000	51.9 per 1,000	12.3 per 1,000	

6. *Effect of Delay in Treatment.*—We have further attempted to determine what effect delay in first aid and delay in hospital treatment and surgery might have on the ultimate production and severity of gas gangrene. MacLennon [1] thinks that the disease develops so soon after wounding and runs so swift a course that delays and difficulties of treatment in the field are not the principal reason for its high incidence and mortality. However, this opinion is not commonly held. A thorough individual interrogation of 73 of the total number of 96 patients was made to determine the effect of this time relationship and was directed along the following lines: Questions were asked each patient concerning the exact time the wound occurred, the type of dressing applied and whether sulfonamides were used according to present army directives. The answers, in general, were definite and accurate, and data thus obtained were correlated with the emergency medical tag, the time of admission to the hospital and the time surgical operation was performed. This was tabulated, as previously, according to nationalities and contrasted with the incidence per thousand surgical cases, as determined in table 1. The data are set forth in table 3.

The shortest lapse of time between initial injury and the development of a true, severe gas gangrene infection occurred in an American soldier who, when operated on only six hours after having received a severe lacerating wound of the right thigh, was found to be thoroughly infected with the organisms. This case is to our knowledge the earliest case of gas gangrene reported. The longest time lapse between injury and surgery was in a German prisoner who lay wounded and unattended for thirty hours and who did not reach

the hospital until four days after injury. It was necessary to treat him medically for three additional days before operation could be performed because of his poor physical condition.

Actually we have not been able to determine over our entire period of activity the average time for cases in which gas infection did not develop to reach operation. As in the cases of those which did, this time lapse in the hospital was dependent on our backlog. Sample tests at the various installations, however, point to the fact that this delay was in excess of eighteen hours.

While the entire period from wounding to débridement is of vital importance in the development of gas gangrene, there can be no question that the time between the occurrence of the injury and the application of the initial dressing is the critical period. This is well exemplified by the present study. This average initial time lapse for the American wounded was twelve minutes, for the Free French eighteen minutes and for the prisoners of war five hours and forty minutes. It is during this period when the wound lies open, in contact with clothing, dirt and soil, that the infection is most likely to be introduced.

Similarly, this is reflected in the time interval which occurred between wounding and arrival at the hospital. An average of fifteen hours elapsed before Americans and French were admitted, while 42.6 hours passed before Germans were delivered to the hospital.

Further study of table 3 shows the same trend while at the hospital itself. The average length of time from injury to operation in the American and French groups was one and one-half days, in the prisoner of war group three and three-fourths days. The peak of American and French operations for gas infection was between one and two days after wounding, whereas in the German group, in which the delay was longer, it occurred between three and four days after wounding This in no way can be thought of as discrimination against the Germans. The delay here was necessarily greater because, in general, the Germans already showed more manifest signs of toxemia and cachexia and most of them needed considerable therapy before being able to withstand surgery. The importance of delay in both initial and definitive treatment is evident when a comparison of the prisoners of war group, with an incidence of 52 per thousand cases, is made with the incidence of 8.0 per thousand cases in the American group.

7. Early Use of Sulfonamide Compounds.—The higher incidence in the German group at one time was thought to be due to the absence of the initial use of the sulfonamides both locally and by mouth. After questioning a number of gas gangrene infected prisoners we were surprised to note that the number of Germans who received sulfonamide therapy from the very beginning almost equaled the number of Americans. All of the former received initial care by American Medical Aid men. All patients received sulfonamides at the hospital. Table 4 demonstrated the result of questioning along these lines.

Since, then, general health factors being equal and sulfonamides being used almost equally in the Allied and German groups, the main factor which could be proposed as having an effect on the development of gas gangrene is the time lapse between wounding and both initial therapy and definitive surgery.

Another factor has recently been noted which may in part also explain the greater incidence of gas gangrene among the prisoners of war. This is the observation, made at operation, that the wounds in this group of patients were much more highly contaminated by shreds and even large pieces of woolen clothing than were the wounds of either American or French soldiers. In checking this we have found that all the garments of the Germans in general showed greater evidence of wear, a greater friability and a much looser nap.

8. Types of Wounds.—Regardless of the gas infection, all wounds were classified as "severe" in the amount of damage produced. Twenty-eight (29 per cent) were of the penetrating type, with metallic fragments present in the tissue; forty-one (43 per cent) were of the perforating type, and the remainder (twenty-seven, or 28 per cent) were lacerating in character. Compound comminuted fractures were present in fifty-six (58 per cent) of all injuries.

9. Location of Infection.—We have analyzed all the injuries in which gas infections developed and divided them into five categories according to location: (1) shoulder, (2) upper extremity (which includes the upper arm, the forearm, the wrist and the hand, (3) buttocks, (4) thigh and (5) lower extremity (which includes the calf, ankle and foot). Multiple wounds were common (60 per cent), but for the purpose of this discussion only wounds infected with gas gangrene are considered. In only 1 case in which multiple wounds were present was gas bacillus infection present at more than one place. A study of all operative diagnoses over the four months of activity was made according to the listing given and the incidence of each type

TABLE 4.—*Sulfonamide Therapy Before Hospitalization*

	United States			Prisoners of War			Free French			Civilians		
	No. of Cases			No. of Cases			No. of Cases			No. of Cases		
	Number Questioned	Receiving Treatment	Per Cent	Number Questioned	Receiving Treatment	Per Cent	Number Questioned	Receiving Treatment	Per Cent	Number Questioned	Receiving Treatment	Per Cent
Sulfanilamide crystals in wound	28	20	71	43	24	55	8	8	100	2	0	0
Sulfonamides by mouth at initial dressing	28	24	82	43	24	55	8	8	100	2	0	0
Sulfonamides by mouth every four hours until hospitalization	28	16*	57.1	43	20*	46.5	8	3*	37.5	2	0	0

* As nearly as can be determined. Cases in which decidedly irregular doses of sulfonamide orally were given are not included in these results.

TABLE 5.—*Incidence of Gas Grangrene According to Site of Infection*

	No. of Cases of Injury	No. of Cases of Gas Gangrene	Per Cent of Total Gas Gangrene	Incidence per 1,000 Injuries
Shoulder	704	8	8.33	11.2
Upper extremity	1,651	17	17.7	10.3
Buttock	483	27	28.1	55.4
Thigh	940	35	36.5	37.2
Lower extremity	1,201	9	9.4	9.7

of wound determined. Similarly the incidences of gas gangrene for the several locations were computed. These interesting statistics are presented in table 5.

By making a classification of all such cases of infection with gas gangrene, and by comparing these with the total number of injuries which have been classified similarly, the sites of predilection for the development of the disease were determined. Thus, while wounds of the buttocks made up slightly less than a third of our series, the incidence of gas infection in buttock injuries was 55.4 per thousand. A like finding is recorded in the case of wounds of the thigh, in which the incidence was 37.2 per thousand. On the other hand, wounds of the shoulder, the upper extremity and the lower extremity below the knee are less commonly infected. We have not, in this hospital, encountered any cases of primary gas bacillus infection of the neck, head, abdomen, back or perineum. Three cases were noted in which gas infection was present in a wound of an extremity and had spread to the trunk.

TREATMENT OF GAS GANGRENE INFECTION

The treatment followed in this series of cases is essentially that which is outlined in U. S. Army Circular Letter No. 178. Many modifications were and still are being made, and attempts at improving our technic and mortality rate are constantly being tried. These modifications and changes are reflected in the constantly decreasing mortality and morbidity as we have proceeded from one installation to another. For example, in our last installation there was only one death in 22 cases, and the average time for evacuation of gas cases was only slightly longer than for the average case without infection. This may be compared to our first setup, in which there was a mortality of 1 in 6 cases and the evacuation time was several days longer than for the average.

Treatment was divided into three stages, the preoperative, operative and postoperative. It was further classified as specific and nonspecific, the specific consisting of the use of penicillin and gas gangrene antitoxin, employed by various methods and utilizing various routes of introduction. Nonspecific measures consisted of general supportive treatment and the use of whole blood, blood plasma and sulfonamides.

1. *Preoperative Treatment.* — During periods of extreme activity, abdominal, chest and brain injuries received priority in surgery. However, when a preoperative diagnosis of gas gangrene infection had been made, regardless of the location of the wound, that case was also given the highest priority rating. The main essential of preoperative care was preparing the patient for débridement as quickly and as completely as possible. General supportive measures, treatment of shock and elevation of the blood count to as near normal as possible were considered to be of primary importance before the patient was ready for operation.

As is well known, the anemia resulting from gas gangrene toxemia is severe. We have noted repeatedly that when the blood count before operation was above 3.5 million, with a correspondingly high hemoglobin value, the traumatic shock occurring from extensive débridement was not as great as when lower blood values were present. We further noted that the patient was returned to the postoperative ward in better general condition, and postoperative therapy was greatly facilitated, when the blood picture approached normal before operation.

Thirty-one patients of this series were admitted to the hospital in shock. Excluding these, whole blood in quantities of from 500 cc. to 2,000 cc. (average 875 cc.) was administered preoperatively to 41 of the 65 remaining patients. Similarly, blood plasma in amounts ranging from 250 cc. to 750 cc. was given to 53 patients (average 400 cc.). Routine blood counts were not made preoperatively but are available for 23 cases. The average for these was a red blood cell count of 3.77 million with a hemoglobin (Tallqvist) of 80.5 per cent either after transfusion had been completed or immediately before operative procedures were started.

Sulfadiazine or sulfathiazole was administered by mouth routinely to all patients, starting with an initial dose of 2 Gm. and continuing with 1 Gm. every four hours. No basic difference was noted in the effects of these two compounds. Medication was continued up to the time the patient was admitted to surgery, and also routinely postoperatively until the patient was evacuated. The amount of sulfonamide drug varied from 3 Gm. minimum to 31 Gm. maximum. The average dose for the 96 patients was 10.2 Gm. preoperatively. No demonstrable effect of the sulfonamide compounds could be observed either in preventing the onset or in limiting the spread of the gas bacillus infection. Its general efficacy against other wound contaminants was easily recognized.

The sodium salt of penicillin was also used routinely postoperatively and was administered by intramuscular injection only. If, for any reason, operation had to be delayed, all patients with wounds of the buttock, thigh and perineal regions received 40,000 units every four hours. More recently we have given 20,000 units at two hour intervals, because when given in smaller and more frequent doses the blood level remains higher. All patients with other extremity and trunk wounds received 20,000 units every four hours. When gas gangrene had been tentatively diagnosed, the patient received the larger dosages regardless of the location of the wound. The smallest dose administered preoperatively was 20,000 units, the largest 960,000 units. The average amount of penicillin given preoperatively was 220,000 units. Although there was no way of determining exactly, we have not felt that penicillin per se had any major effect preoperatively in preventing the infection, in decreasing its severity or in preventing its spread.

The use of gas gangrene antitoxin preoperatively has not proved very successful in our hands. Arbitrarily, eighteen therapeutic doses were given in 4 cases in which it was thus used. In these cases, no appreciable change was observed; the toxicity was not relieved, nor was the postoperative course affected favorably in any manner. In 1 case a pronounced sensitivity to the serum developed, and it was necessary to desensitize the patient before more of the antitoxin could be given postoperatively. Furthermore, adequate or complete dosage could not be determined, as we were able to do postoperatively in a large number of cases. Therefore, since we felt that as it was not efficacious preoperatively, and since a certain amount of unnecessary harm could be done by administering large amounts of foreign protein unnecessarily, the injection of antitoxin before operation was discontinued.

2. *Operation.*—We have confirmed, and it is not possible to overemphasize the fact, that early surgical débridement is the one single measure of vital impor-

tance in the prophylaxis as well as the treatment of gas gangrene. That such treatment should be completed as early as possible after the wound has occurred is demonstrated in table 3. Furthermore, we have noted repeatedly that, when operation was delayed for long periods the toxicity postoperatively was both deeper and prolonged and that the degree and intensity of the morbidity was likewise increased. We have estimated that the average time for all gas gangrene patients, regardless of nationality or the press of large numbers of patients to reach operation, after wounding was 3.1 days from the time that they were wounded. In order to emphasize the effect of this delay, in six of the eleven deaths which occurred directly as the result of gas gangrene the average wait before operation was longer than 5.2 days.

Not only is early surgical intervention important but also a thorough complete débridement of the wound is essential in the successful treatment of the disease. Reports of case histories of gas gangrene in the closing year of World War I have demonstrated this. Similarly a private communication from one of the nurses stationed at Corregidor prior to its fall in 1942 stated that gas gangrene was being handled quite successfully by extensive débridement and that neither sulfonamides, penicillin nor in many cases whole blood was available.

In accord with the best surgical principles, we have found that in operating on patients with patent gas gangrene, all foreign bodies, metallic as well as nonmetallic, such as splinters, pieces of clothing and dirt, had to be removed to prevent recurrence. Likewise, all damaged and infected muscles or muscle groups had to be cut away. Counterincisions to promote aeration and drainage have been employed more and more. From time to time, in hopes of saving a badly injured extremity, amputation was held off in spite of definite interference with blood supply. This was justified by the saving of an appreciable number of limbs. However, in a few cases in which the circulation was inadequate and moist gangrene supervened, pockets of gas infection were found at the time of amputation. Such cases constitute 3 of the 6 instances in which gas gangrene developed subsequent to primary operation. The importance of thorough débridement and likewise the secondary role of the chemotherapeutic agents with grossly incomplete operation is well exemplified by the following case:

Case 34.—A private first class was wounded by a shell burst and shrapnel fragments on Oct. 6, 1944 at 10 a. m. Five minutes after he received his injury the wounds were dressed by medical aid men but no sulfanilamide powder was introduced. Sulfadiazine 3 Gm. was taken by mouth. The injuries consisted of extensive and numerous penetrating wounds of the right thigh, leg, foot and also the right arm. These wounds were complicated by compound comminuted fractures of both the right fibula and the right radius. Plasma 500 cc. was administered between the time the wound was dressed and 8 p. m., when he was received at this hospital.

During the twelve hours he remained in the preoperative ward he received 1,000 cc. of whole blood, 500 cc. of plasma, 5 Gm. of sodium sulfadiazine intravenously and 120,000 units of penicillin intramuscularly. Extensive débridement of all wounds was carried out at 8 a. m. October 7, twenty-two hours after being wounded. At this time the circulation of both the leg and the arm was good. Many pieces of shrapnel were removed and much muscle tissue was excised, but no suspicion of gas infection was noted. Because of the vastness of the injury the surgeon felt that the débridement was incomplete.

On the evening of the second postoperative day the soldier complained of severe pain in the right foot and leg. The temperature and pulse rate, which previously were normal, began to rise the following morning.

At 9 p. m. October 10 he was taken to the operating room for inspection of the wound. At this time moderately extensive evidence of gas gangrene (gas bubbles, myositis and edema) was found in the right thigh. Muscle smears at this time were positive. Amputation was performed above the level of the infection. The condition of the wound of the arm was good. Between the first and second operations he received 960,000 units of penicillin, 31 Gm. of sulfadiazine, 500 cc. of whole blood and 500 cc. of plasma.

There is no question that because of the extensiveness of the leg wound and because of the inability of the operator to remove all necrotic and dead tissue the gas infection was able to spread. Notes of incomplete débridement because of poor physical condition or because of critical systemic complications in the general condition of the patient were made in 2 other of the 7 cases in which gas gangrene developed postoperatively.

Routinely, approximately 5 Gm. of sulfanilamide crystals was dusted into wounds after the operation was completed. The maximum employed was 7 Gm., the minimum 4 Gm. We have found, as have others, that it was necessary only to dust the wound and that larger amounts caked and prevented drainage.

At the onset of this study, penicillin was not used routinely at the site of the injury. It was not until approximately two thirds of this series was completed that penicillin was used locally at the time of operation. We had felt that the rapidity of absorption of this drug was so great that local use was of no great importance. However, since dusting penicillin into the wound has become routine we have found that the length of postoperative morbidity has been decreased and that the postoperative course has been less stormy. It may be conjectured, since the gas bacillus grows in dead or dying tissue where the blood supply is absent or minimal, that penicillin given systemically cannot reach the infected area but that by local use the direct effect of the drug is utilized. When penicillin was employed locally it was mixed with the sulfanilamide before being placed in the wound. Twenty-two cases were thus treated with doses of from 33,000 units to 100,000 units dusted in the wound.

3. *Postoperative Treatment.*—Practically as important as the actual procedure was the care and therapy of the patient after reaching the postoperative ward. Treatment had to be carefully balanced between the condition of the patient and the amount of medication necessary.

Sulfonamides were used routinely in doses of 1 Gm. every four hours by mouth, or comparable doses intravenously when the oral route was not available. Although we, as most others,[2] feel that the sulfonamides have no effect against the clostridial organisms, they have a definite place in the therapy of gas gangrene because of their bactericidal or bacteriostatic effect on other virulent and putrefactive organisms. Sulfadiazine was given preference over sulfathiazole, since fewer side reactions were encountered, and was continued rou-

2. Hac, L. R., and Hubert, A. C.: Proc. Soc. Exper. Biol. & Med. **53**: 61, 1943. McKnight, W. B.; Loewenberg, R. D., and Wright, Virginia L.: Penicillin in Gas Gangrene, J. A. M. A. **124**: 360 (Feb. 5) 1944.

tinely from the time the patient was returned from operation until he was evacuated or until special orders for discontinuance were written. The minimum dose postoperatively was 8 Gm. given to 2 patients who died within twelve hours of operation; the maximum was 60 Gm. The average amount administered was 26.3 Gm.

The most consistent characteristic effect of the toxemia resulting from the infection was the severe anemia produced in all cases. Eventually we discarded several cases from this series because both the toxemia and the anemia were absent. To our mind, both these factors must be present to verify any diagnosis of gas gangrene. This anemia was particularly severe and very difficult to combat. The average postoperative blood count was slightly under 3 million red blood cells per cubic millimeter, with a corresponding hemoglobin average of 62 per cent. Counts as low as 1.5 million were not exceptional. It was necessary to use whole blood in large amounts and at frequent intervals to combat this anemia. Over the entire series an average of 2.7 transfusions of 500 cc. of citrated blood was given. The maximum administered was 5,000 cc. over a period of seven days. Transfusion reactions were more common but not more severe with these patients than with average cases throughout the hospital. In general these consisted of mild to severe chills, with various degrees of hyperpyrexia, urticaria and in 1 case hemoglobinuria and oliguria. All such reactions subsided with appropriate therapy.

Furthermore it was noted that the result of a single transfusion was not nearly as permanent as might be expected. Increases in blood counts and hemoglobin noted a few hours after having received blood were almost obviated twenty-four hours later. This was not nearly as pronounced when the severity of the toxemia abated and may be interpreted as being due to the increased hemolytic effect of the toxins on blood cells, whose fragility may have been increased by standing in vitro.

The specific treatment of gas gangrene infection consisted in the active and aggressive use of penicillin and gas gangrene antitoxin, the former for its action against the organism themselves and the latter for overcoming the toxins produced by them. From the very beginning of this work our observations pointed to the fact that penicillin was active in combating clostridial infections only after débridement had been completed and when minimal foci were present. As our experience increased we felt more and more strongly that the amount of penicillin necessary to combat the infection successfully was insufficient and had to be increased. With the first half of this series an average of 480,000 units was given postoperatively, whereas in the second half an average of 730,000 units was administered. Several patients received as high as 1,200,000 units. At first this was all given intramuscularly. To provide a more rapid increase in the blood level we have recently begun to use penicillin intravenously, independently of the intramuscular route, in doses of 40,000 units together with the intravenous administration of gas gangrene antitoxin, as described in subsequent paragraphs.

Gas gangrene antitoxin was administered to 82 of the 96 patients in doses of from one to forty-four therapeutic doses. The term "therapeutic dose" is used to signify the amount of trivalent gas gangrene antitoxin which contains 10,000 units each of the antitoxins for Clostridium welchi and Clostridium septicum together with 1,500 units of the antitoxin for Clostridium oedematiens. Although Army directives state that eighteen therapeutic doses should be administered in every case, we have modified this procedure and attempted to regulate the amount given by the degree of toxemia. In our experience the antitoxin per se did not seem to have any inhibitory effect on the organisms themselves but was very efficacious against the toxins produced by the infection. To illustrate this the following case history is quoted:

CASE 54.—A private first class was wounded at 4 p. m., Nov. 9, 1944. The wound was dressed with sulfanilamide powder about ten minutes later. Sulfadiazine 3 Gm. was also taken by mouth. The patient was transferred to this hospital at 12:55 p. m. November 10. A tentative diagnosis of gas gangrene infection in a severe penetrating wound of the left thigh was made on admission.

Preoperatively he received 160,000 units of penicillin and 9 Gm. of sulfadiazine. At operation, ten hours after admission, an extensive débridement, with removal of many large metal fragments, was performed. Considerable devitalized, gray, necrotic and edematous muscle tissue was removed. Both muscle and exudate smears were positive. Two counterincisions, one on the medial and one of the posterior aspect of the thigh, were made to insure adequate exposure and drainage; 33,000 units of penicillin and 5 Gm. of sulfanilamide were dusted into the wound.

The patient was returned to the ward in a highly toxic and irrational state. His temperature was 103 F., pulse rate 180, hemoglobin 55 per cent, red blood cell count 2.7 million. Five hundred cc. of whole citrated blood was given, which was followed by an intravenous drip of nine therapeutic doses of gas gangrene antitoxin together with 40,000 units of penicillin over a period of three hours. A severe, generalized urticaria developed but the mental cloudiness partially disappeared. Following this another 500 cc. of blood was given and then another nine therapeutic doses of gas gangrene antitoxin together with 40,000 units of penicillin. Outside of an increase in the urticaria, the condition of the patient improved remarkably. He became mentally normal and the temperature dropped to 99.8 F. but the pulse rate remained high.

Antitoxin one therapeutic dose was given intramuscularly every twelve hours for four doses. Penicillin was also administered intramuscularly in doses of 20,000 units every two hours for a total of 480,000 throughout the entire time. Two transfusions totaling 1,000 cc. of whole blood were also given. Forty-eight hours after the intravenous antitoxin was completed the pulse rate and temperature rose and the patient was returned to the operating room for inspection of the wound. No change in the mental state was noted. On examination, a subcutaneous crepitus was present which extended to the axilla. Extensive longitudinal incisions were made and débridement of the infected tissues was carried out. Since he was moderately toxic on return to the ward it was necessary to give eighteen additional therapeutic doses of gas gangrene antitoxin intravenously over a period of six hours. These completely controlled the toxic state. He was evacuated on the seventh postoperative day. A total of forty therapeutic doses of antitoxin, 3,000 cc. of whole blood, 960,000 units of penicillin intramuscularly and 120,000 units intravenously and 31 Gm. of sulfadiazine were administered. Recovery from gas infection was complete as far as known.

Thus it is obvious that the antitoxin was able to control the toxemia in this case despite the fact that the organisms were still present and active in the wound. Likewise, despite the administration of the antitoxin, the organisms themselves were not inhibited. This was noted in all our cases which, when diagnosed

at the time of operation, required further operative procedures because of the spread of the infection. Such striking effect of antitoxin therapy did not occur in every case, but in a large majority we were able actually to gage the amount necessary by the response to the drug. If no untoward reactions developed with its use we usually considered eighteen therapeutic doses to be a minimum. However, no figure can be given for the total dosage which may be necessary to neutralize the toxin.[1] The following case summary illustrates the manner in which we have attempted in general to judge the amount of gas gangrene antitoxin necessary:

CASE 73.—A prisoner aged 42 presumably was wounded several days before he was picked up by American troops at 2:35 p. m. Sept. 14, 1944. There were dirty dressings covering multiple penetrating wounds of the left buttock and thigh, which were complicated by a severe compound comminuted fracture of the left femur. Wounds of the right calf and right foot also were covered with dirty dressings. All injuries were dusted with sulfanilamide and redressed, and 3 Gm. of sulfadiazine was given by mouth. Plasma 250 cc. also was administered at this time. He was evacuated to this hospital at 12:20 a. m. September 15.

On admission a blood pressure of 68/40 was recorded. Diagnoses of severe shock and of extensive gas gangrene of the left lower extremity were made. The patient was extremely toxic and irrational. The red blood cell count was 2,100,000. Hemoglobin was 50 per cent. Despite the administration of large amounts of fluid intravenously it was impossible to raise the blood pressure to normal limits for any length of time. During the forty-eight hours of preoperative therapy he received 2,000 cc. of whole blood, 2,000 cc. of plasma, 2,000 cc. of glucose 5 per cent in saline solution, 15,000 units of tetanus antitoxin, 440,000 units of penicillin and 8 Gm. of sodium sulfadiazine. Because of increasing coma and toxemia, and because of decreasing resistance, it was decided that operation was necessary, in spite of the precariously low blood pressure.

The patient was admitted to the operating room at 4 a. m. September 17. A high guillotine amputation of the left thigh was performed because of extensive loss of bone and extensive gas gangrene in the entire thigh and calf. Gas was found to extend into the abdominal wall above Poupart's ligament and to the entire left buttock region. Five hundred cc. of whole blood, together with 500 cc. of blood plasma was given during the amputation. Because the condition of the patient was becoming more and more critical, only counterincisions were made in the calf and buttock without any major débridements being carried out. Six Gm. of sulfanilamide was dusted into the wound.

On return to the gas gangrene isolation tent the blood pressure was 70/50 mm. of mercury, the red blood cell count 2,000, hemoglobin 50 per cent and temperature 104 F. The patient was toxic and irrational and appeared to be dying. One thousand cc. of whole blood followed by 500 cc. of plasma was introduced under pressure. This was followed by nine therapeutic doses of gas gangrene antitoxin in 700 cc. of saline solution. No appreciable change was noted, and another nine therapeutic doses of antitoxin were given over a period of three hours. The temperature dropped to 102.2° F. and the blood pressure remained constant at 70/50. At this time the patient seemed to be slightly less irrational and also seemed to be resting quietly at times.

Fifteen hundred cc. of blood and 500 cc. of plasma were again given, followed in turn by twelve additional therapeutic doses of gas gangrene antitoxin in 1,000 cc. of saline solution and glucose 5 per cent. Four hours after this was completed there was a noticeable change in the condition of the patient. The mental state appeared more normal, actions became purposeful and there was a general diminution in the toxemia. The pulse rate was 110, blood pressure, 80/60, red blood cell count 2,800,000, hemoglobin 62 per cent and temperature 99 F. Since the patient had not urinated, catheterization was done and 100 cc. of thick viscid urine containing many red blood cells and 3 plus albumin was removed.

During the next twelve hours four additional therapeutic doses of gas gangrene antitoxin were given followed by 1,000 cc. of blood. Despite the facts that the blood pressure still remained at 90/60 and the anuria continued, the general condition of the patient seemed to be improving. To combat the faulty kidney function 500 cc. of 10 per cent glucose was given intravenously throughout the day. One hundred cc. of 50 per cent glucose and aminophylline in 10 cc. doses were also given twice during the twenty-four hour period.

On the third postoperative day the patient was decidedly edematous and began to show signs of uremia. Urinary function was not resumed and the patient died on the fourth postoperative day. During this entire period he received thirty-four therapeutic doses of gas gangrene antitoxin, 960,000 units of penicillin, 15 Gm. of sodium sulfadiazine, 500 cc. of blood plasma, 3,000 cc. of whole blood, 500 cc. of 10 per cent glucose, 300 cc. of 50 per cent glucose and 30 cc. of aminophylline.

Postmortem examination revealed signs of uremia, pulmonary edema and generalized anasarca. No evidence of gas gangrene was found in the amputation stump, and only old necrotic muscle tissue, with no gas involvement, was found in the other wounds.

It is our opinion that death here resulted from uremia following kidney failure which was secondary to the prolonged period of shock, and that, had the patient been able to overcome the anuria, he would also have overcome the gas gangrene infection.

Reactions to the horse serum, despite negative intracutaneous and ophthalmic tests, were common and were noted in 75 per cent of all our cases. These reactions were manifested by urticaria, chills and fever. We felt that because of the severity of the disease itself, as compared with the mildness of the reactions, they were not sufficient indication for cessation of therapy. This was proved repeatedly by experience, and we have felt justified many times in continuing the infusions despite the presence of these untoward effects. However, one severe anaphylactic reaction did occur. This manifested itself by severe respiratory embarrassment, dyspnea, orthopnea, cardiac irregularity with gallop rhythm, cyanosis and, three hours later, death. Epinephrine, ephedrine and aminophylline in large doses intravenously and intramuscularly were not effective. The reaction occurred after approximately 10 cc. (one-half the therapeutic dose) of the antitoxin had been administered.

The following briefly is the general procedure which we have developed, which has proved in our experience to be the most efficacious in the treatment of gas gangrene postoperatively:

1. Sensitivity test for horse serum immediately on return to postoperative ward, 0.1 cc. of undiluted serum intracutaneously and 0.1 cc. of a 10:1 dilution intraconjunctivally.

2. Nine therapeutic doses of gas gangrene antitoxin in 700 cc. of isotonic solution of sodium chloride as a continuous intravenous drip over a three hour period; 40,000 units of penicillin introduced through the rubber tubing at the start of infusion. A rest period of from three to four hours to observe the effect of the antitoxin. If anemia is present, 500 cc. of whole blood to be transfused at this time.

3. Repetition of 2 until signs of toxemia begin to abate. No limit has been set on the number of therapeutic doses of antitoxin to be administered.

4. Penicillin 20,000 units every two hours together with sulfadiazine 1 Gm. every four hours or, if the oral route is not available, 10 to 15 Gm. of sodium sulfadiazine intravenously per day. A minimum of 720,000 units of penicillin, not including that given intravenously, should be completed by the intramuscular route before therapy is completed.

5. One therapeutic dose of antitoxin every twelve hours intramuscularly after the completion of the intravenous therapy for a minimum of four injections.

6. Hemoglobin, red blood cell count, hematocrit, intake and output checked daily; whole blood as necessary.

Criteria of Cure.—In many cases it was difficult to evaluate a cure because it was often necessary to evacuate patients before we were sure that the disease was completely eradicated. Criteria therefore were limited to examination of the wounds to determine if further extension had taken place or to see if the wound was clean. Besides this, temperature and pulse had to be normal and all evidences of toxemia eliminated. Muscle smears were not made at time of inspection of the wound.

Mortality.—As has been stated, we have attempted to maintain a rigid and high standard of diagnosis. To the best of our medical and surgical knowledge all patients in this series treated for gas gangrene infection actually were infected with a virulent form of the disease. Likewise "prophylactically treated" cases or doubtful cases are eliminated from the scope of this discussion.

In an evacuation hospital, patients are rarely kept for long periods of time, but they are evacuated as soon as the surgeon considers them to be transportable. For this reason, and also because of the military situation, it was often necessary to evacuate patients before a definite cure could be determined. However, follow-up cards were included in each jacket as the patient was evacuated. The cooperation of medical officers in rear echelons has been excellent, and all cards of cases in which the outcome was doubtful have been completed and returned.

TABLE 6.—*Postmortem Findings in 15 Cases*

	Cases
Death due to anaphylaxis and serum reaction, gas gangrene still present in tissues	1
Death due to peritonitis from intestinal wounds, gas gangrene not found post mortem	2
Death due to traumatic irreversible shock, gas gangrene not present post mortem	1
Death due to anuria following profound prolonged irreversible shock, gas gangrene not present post mortem	1
Death due to uncontrolled gas gangrene infection (4 cases proved post mortem)	10

To the best of our knowledge, 15 patients of the entire series of 96 have died. Postmortem examinations were completed in about one half of these cases. When a postmortem examination was not made, the death was classified as being due to gas gangrene. A summary of these postmortem findings is included in table 6.

Thus, no pathologic evidence of gas gangrene could be found in 4 of the total of 15 cases in which death occurred after treatment for gas gangrene infection. All of these cases had complete anti-gas gangrene therapy before death. They can therefore be deleted, thus making the mortality rate for the series of 96 cases 11.5 per cent.

COMMENT

Various interesting data have been derived from this statistical and therapeutic discussion of a series of 96 cases of "clinical gas gangrene" treated in an evacuation hospital in northern France during the four months beginning July 25 and ending Dec. 1, 1944. An incidence of 16.0 cases per thousand surgical admissions with a mortality rate of 11.5 per cent has been noted. These cases represent not only American but also Free French, French civilian and prisoners of war casualties.

With the criteria for the diagnosis of gas gangrene, both preoperatively and at the time of operation, that have been outlined, as a basis, 35.4 per cent of our cases were diagnosed before reaching the operating room; 57.4 per cent were first noted at the time of operation; the remaining 7.2 per cent developed the infection postoperatively.

The highest incidence of gas infection (52 per thousand surgical cases) was found in the prisoner of war group. This was six times higher than the American (8.0 per thousand), four times higher than the Free French (12.3 per thousand) and seven times greater than the civilian (7.8 per thousand). This was probably due to delay in the initial dressing of the wound and also to the delay between wounding and definitive therapy. Evidence tended to point to the increased fragility and friability of the German clothing and the larger amounts of this clothing found in the wounds.

As has been suggested previously (Bailey [3]) we have shown that wounds of the buttocks were most prone to develop gas gangrene (55.4 per thousand cases), those of the thigh next (37.2 per thousand cases), shoulder (11.2 per thousand cases), upper extremity (10.3 per thousand cases) and leg (9.7 per thousand cases).

Active treatment of gas gangrene infection must begin early to produce maximal beneficial effects. Once clinical gas gangrene has developed, the therapy must center around radical surgery, laying the wound wide open, the lavish use of counterincisions and, if necessary, amputation of the part. In the entire series five upper extremities and seven lower extremities were amputated for this reason.

Surgery alone, however, was not completely efficacious in treating the infection. Sulfonamides, penicillin and gas gangrene antitoxin, together with the use of vigorous supportive measures, were of inestimable value in the saving not only of limbs but also of lives.

From our observations we have felt that the sulfonamide compounds were of little value against the clostridia themselves but had tremendous therapeutic effect against other contaminants of the wound. This is in agreement with many other observers. Hac and Hubert,[2] McKnight, Loewenberg and Wright [2] and others have demonstrated the inefficacy of sulfonamide compounds against the gas gangrene infection in both in vivo and in vitro experiments.

The value of penicillin has been a question for some time. There is no doubt that penicillin alone, or even complemented with gas gangrene antitoxin, is insufficient to inhibit the disease once infection has set in and has begun to spread. In vitro experiments [4] held promise that this drug would be of value in the treatment of clostridial infections. Animal experiments with penicillin have not carried over completely to man, and Keefer, Blake, Marshall, Lockwood and Wood [5] indicate that more clinical observation is needed in human cases before adequate conclusions may be drawn.

3. Bailey, Hamilton: Surgery of Modern Warfare, 1944, vol. 2, p. 275.

4. Abraham, E. P.; Chain, E.; Fletcher, C. M.; Gardner, A. D.; Heatley, N. G.; Jennings, M. A., and Florey, H. W.: Lancet **2**: 226, 1940. Chain, E.; Florey, H. W.; Gardner, A. D.; Heatley, N. G.; Jennings, M. A.; Oer-Ewing, J., and Sanders, A. G., ibid. **2**: 226, 1940. McIntosch, J., and Selbia, F. R., ibid. **2**: 750, 1942.

5. Keefer, C. S.; Blake, F. G.; Marshall, E. K. Jr.; Lockwood, J. S., and Wood, W. B., Jr.: Penicillin in the Treatment of Infections, J. A. M. A. **122**: 1217 (Aug. 28) 1943.

Jeffrey,[6] Cutler[7] and Harvey and Meleney[8] were disappointed with the effect of penicillin when used against Cl. sordelli and Cl. welchi. On the other hand, Herrell, Nichols and Heilman,[9] Kepl, Ochsner and Dixon[10] and others are satisfied that this drug is satisfactory in the treatment of the infection. We, from our observations, are heartily in accord with the latter. Penicillin in large doses, both locally, intramuscularly and intravenously, has helped in the reductions of both mortality and morbidity of the disease.

We furthermore are in accord with Herrell[9] and the British investigators[11] that penicillin alone is not efficacious and that it must be combined with the antitoxin and surgical operation. While penicillin may definitely inhibit the growth of the organisms, the neutralizing effect of the antitoxin is essential for the cure of the disease. However, we have found that the preoperative use of the antitoxin is not to be recommended. Moreover, we have been able in most of our cases to determine the amount of antitoxin needed postoperatively by judging the effect on the clinical course of the toxemia.

SUMMARY

1. Ninety-six cases of clinical gas gangrene infection were treated at an evacuation hospital in four months of service in northern France, an incidence of 16.0 per thousand battle casualties.

2. The incidence of gas gangrene was highest in the prisoners of war (62 per thousand battle casualties) and was considerably lower in Americans and Free French (9.9 per thousand and 12.3 per thousand respectively).

3. The development of gas gangrene is influenced by the time interval between the initial wound and the primary first aid dressing; also by the delay in accomplishing definitive surgery.

4. Gas gangrene is most prone to develop in wounds of the buttocks, thighs, shoulder and upper and lower extremities in the order named.

5. Radical, extensive, thorough and early surgery is the most important factor in the prophylactic and therapeutic treatment of gas gangrene.

6. Sulfonamides, both locally and by mouth, have little or no effect on the development of gas gangrene.

7. Penicillin in large doses was found to be an excellent adjunct in the chemotherapeutic treatment of gas gangrene. It is not sufficient in itself to control the infection but, when used in conjunction with surgery and antitoxin, has been of inestimable value.

8. Gas gangrene antitoxin appeared to have little value preoperatively. Its main value is the neutralization of the toxemia postoperatively. Furthermore, little effect against the organisms themselves was noted. The dosage could not be dogmatically determined, since it varied with the degree of toxemia. A minimum of eighteen therapeutic doses is recommended when no sensitivity or other contraindication is found.

9. Eleven patients of the total of 96 died as the direct result of gas gangrene infection, a mortality rate of 11.5 per cent.

6. Jeffrey, J. S.: Brit. M. J. **2**: 656 (Nov. 20) 1943.
7. Cutler, E. C.: Brit. M. J. **2**: 655, 1943; J. A. M. A. **124**: 117 (Jan. 8) 1944.
8. Harvey, H. D., and Meleney, F. L.: Surgery **15**: 622, 1944.
9. Herrell, W. E.; Nichols, D. R., and Heilman, Dorothy H.: Penicillin, J. A. M. A. **125**: 1008 (Aug. 12) 1944.
10. Kepl, Maxwell; Ochsner, Alton, and Dixon, J. L.: Two Cases of Clostridium Welchi Infection Treated with Penicillin, J. A. M. A. **126**: 96 (Sept. 9) 1944.
11. Discussion on Penicillin, Lancet **2**: 638, 1943.

THE TREATMENT OF CERTAIN TYPES OF FRACTURES

WITH A V2A STEEL NAIL IN THE MEDULLARY CAVITY (THE KÜNTSCHER METHOD)

B. M. TORDOIR, M.D.
AND
E. J. MOEYS
Surgeon and Fellow of Surgery, Respectively
NYMEGEN, THE NETHERLANDS

Böhler[1] in his book predicted that "advances similar to the Sven Johansson treatment for fractures of the neck of the femur would enable us in the future to treat certain types of fractures of other bones in the same way." His words came true when in 1940 Küntscher[2] introduced his method. His experiments on animals had proved that fractures of the shaft of the long bones had healed very nicely by putting a V2A nail in the medullary cavity through a small opening in the epiphysial end. Since then he has treated many cases with excellent results and in 1944 Böhler published a third volume to his book giving the results in 500 cases.

As the nail finds its fixation in both the epiphysial ends without injuring the articular cartilages (in children great care should be taken to avoid the epiphysial disk) it will be understood that the best type of fracture for this method is the transverse one in the diaphysis. The nail in these cases gives a very exact reduction without chance for displacement. A few days after the operation—which should be done as soon as possible after the accident—the patient is able to walk about and to leave the hospital. In particular to elderly people this means a great advantage as it prevents a stiffening of the joints, atrophy of the muscles, decubitus and hypostatic pneumonia. The exact reduction of the transverse fracture with its frequent great displacement of the fragments and the quick mobilization form the best indication for the use of the Küntscher nail. In the more oblique type of diaphysial fractures only the exact reduction is in some cases already an indication. For compound fractures—if treated within the time limit of six to ten hours—the same indications are of value. Excellent results are also reached in the treatment of pseudarthroses, provided the fibrous tissue is removed and fresh bone surfaces are approximated.

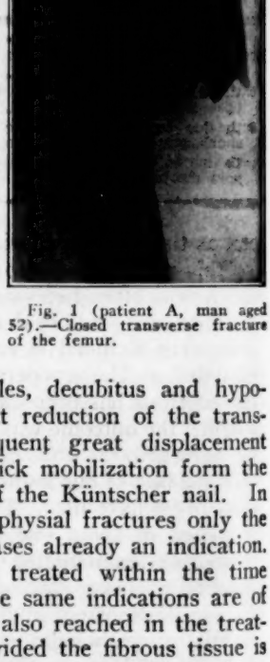


Fig. 1 (patient A, man aged 52).—Closed transverse fracture of the femur.

Küntscher and later his collaborators (Maatz) used nails of different form and sizes in accordance with the type of bone. For the femur they use a straight type of nail and for the tibia and humerus a slightly curved one. Before the operation a very exact x-ray examination should be made of the width of the medullary cavity and the length of the bone. The reduction of the fracture

A more extensive publication on this subject will appear shortly.

From the Surgical Department of the St. Canisius Hospital, Nymegen (in the already liberated part of the Netherlands).

1. Böhler, L.: Technik der Knochenbruchbehandlung im Frieden und im Kriege, Vienna, Wilhelm Maudrich, 1942-1943.
2. Küntscher, G.: Zentralbl. f. Chir. **67**: 1145 (June 22) 1940; **69**: 1837 (Nov. 21) 1942.

is done with the help of a special frame under fluoroscopic control, and special attention should be given not only to the exact reduction of both the fractured ends but also to the exact reduction of the axis of the whole bone in regard to the axial fixation of the nail in the spongy substance of the distal epiphysis. For the femur an opening is made in the trochanteric fossa just medial of the greater trochanter with a piercer, and a thin stiff nail is pushed toward the medullary cavity beyond the fracture into the distal fragment. Then the Küntscher nail is slipped over the thin wire, which then will be removed. For the tibia a weak spot just above the tuberosity and in fractures of the humerus both the epiphyses are used.[3]

As will be easily understood, a complete set of instruments and a large collection of nails, an excellent x-ray equipment, reduction frames and an extensive experience are needed if good results are to be obtained. X-ray controls in connection with the formation of callus must be made at regular intervals to determine the date of the removal of the nail. Through a small incision the perforated head of the nail, which all the months needed for consolidation remained outside the bone, is "hooked" with a special instrument, and without any force the nail is easily removed.

Though the method introduced by Küntscher is an operative one, the extent of the operation is limited to a very small incision at the epiphysial end at the time of the application and the moment of the removal of the nail. Any type of anesthesia which gives complete relaxation of the muscles may be used.

Our own experience with the Küntscher method is a very good one despite the many great handicaps we had and which were due to war conditions. We had at our disposal only a limited number of nails on the one hand and a very large number of war casualties on the other, who arrived in such numbers in our hospital that, even if we had had a sufficient number of nails, we nevertheless could not have handled them all in the required time limit for the treatment of compound fractures. In addition to these disadvantages we did not have x-ray screens to control reduction during operation, so we decided in some cases to open the fracture and to put the nail in the shaft—in case of a femur fracture in the proximal fragment—and hammered it retrograde in the epiphysis. Subsequently reduction was done and the nail brought in the distal fragment.

Our experience with the Küntscher method may be divided into two groups: (1) closed fractures and (2) compound fractures.

1. We operated on 21 closed fractures of the femur, 5 of the tibia, 2 of the humerus, 2 of both radius and ulna, 2 of the fibula and 2 of the olecranon. Figures 1 and 2 show ideal types of transverse diaphysial fractures of the femur and humerus. These patients, aged 52 and 13 respectively, left the hospital after fourteen and eighteen days.

That also in the spiral type of fracture the result may be excellent is demonstrated by figures 5 and 6, of a spiral fracture of the femur in a child of 12 years, though a quicker mobilization than normal could not be obtained.

In cases of a fracture at the lower and diaphysial end of both tibia and fibula we put a thin V2A steel wire in the medullary cavity of the fibula, then reduced the very often greatly displaced tibia fragments under fluoroscopic control (in the x-ray department of the hospital) and applied a circular plaster of paris cast. To prevent possible formation of a pseudarthrosis (as might be feared to develop with an "intact" fibula) we had the patient mobilized soon after the operation.

In rare cases of epiphysial fracture the nail may be of great value, as is shown in figures 7 and 3 of a subtrochanteric fracture of the femur with a great displacement of the fragments. Fractures of the olecranon may also be treated with a Küntscher nail.

Our 10 compound cases had at the time of their arrival in the hospital a complete revision of the wound

Fig. 2

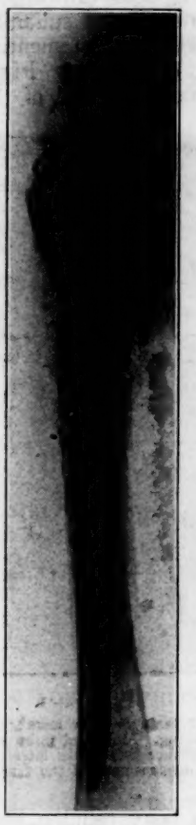


Fig. 3

Fig. 4

Fig. 2 (patient A).—Immediately after Küntscher nail has been introduced: ideal reduction; axis of the bone restored. Fig. 3 (patient C).—Nail introduced: ideal reduction of the fracture shown in figure 7. Fig. 4 (patient D, girl aged 17 years).—Five months after operation, nail having been introduced four weeks after the accident: splendid consolidation; new bone around the nail bridging the defect; function 100 per cent.

—a splint and sulfanilamide locally as well as generally. In this way we were able to prevent infection of the wound to a large extent. If then, sometimes after weeks, we had a nail at our disposal, we placed it in the medullary cavity and covered the periosteum with muscle but left the wound completely open to enable drainage of the wound secretion. Küntscher himself never went so far as to use his method in compound fractures secondarily. Probably he did not have to. But we had many cases with a complete fragmentation of the bone by shell or bomb fragments and a very substantial displacement of the bordering shaft fragments. We expected that the nail, besides an ideal

3. Nordmann: Arch. f. klin. Chir. **200**: 71, 1940.

restoration of the axis of the fractured bone, should enable the formation of new bone substance around that part of the nail which bridges the defect, as at least some of the bone splinters might furnish the necessary osteoblasts.

Other advantages might be obtained: easier and less painful handling of the extremity, the possibility of using the joints, the prevention of atrophy and last but not least the decrease of the wound secretions. In some cases traction should be exercised to forestall the shortening of the bone, which happened sometimes when the muscles retracted the distal fragment to the proximal one, in particular in cases in which a certain area had been split up into many small fragments. Though theoretically we considered the possibility of a developing osteomyelitis outside the place of the fracture, we never saw it happen. In this respect we attached great value to the use of sulfanilamide both locally and generally. All the aforementioned objectives were reached in most of our cases. Figure 4 shows a case of compound splinted fracture of the humerus in a girl of 17 in which bony reunion in ideal position was obtained.

Fig. 5

Fig. 6

Fig. 7

Fig. 5 (patient B, girl aged 12 years).—Four months after operation: perfect consolidation, with full restoration of the anatomy without shortening. Mobilized three weeks after operation; two weeks later, function 100 per cent. Fig. 6 (patient B).—Appearance two weeks later. Fig. 7 (patient C, girl aged 9 years).—Subtrochanteric fracture of the femur with great displacement of the fragments. See figure 3.

Even in late cases of compound fractures the method may prove to be of value.

Ascendency in Medicine.—A distinguished historian recently remarked that few nations which have achieved ascendency in medicine retain that preeminence for more than fifty years. French medicine gained a commanding influence in the Western World during the time of François Magendie; soon after he died, leadership passed largely to Germany; now it has come to England and the United States. Magendie's life coincided with the most critical period of French history: the chaos of the late eighteenth century, the French Revolution and the subsequent rise of democratic government and the appearance of physicians such as Corvisart, Bichat, Laënnec, Louis and Cruveilhier. Then came the rise of scientific medicine associated so intimately with the names of Flourens and LeGallois, but more particularly with the positive leadership of Magendie. —Olmsted, J. M. D.: François Magendie, New York, Schuman's 1944.

THE EFFECT OF PENICILLIN ON HEPARIN TOLERANCE

LAURENCE E. HINES, M.D.
AND
DONALD L. KESSLER, M.D.
CHICAGO

The occurrence of extensive visceral hemorrhages in 2 patients with bacterial endocarditis treated by penicillin suggested this study.

REPORT OF CASES

CASE 1.—Mrs. M. S., white, aged 37, entered St. Joseph Hospital May 5, 1944 because of intermittent chills and fever since November 1943, starting three weeks after the delivery of a normal child; weight loss of 20 pounds (9 Kg.) in six months; sudden onset of right hemiplegia on Jan. 30, 1944, which had improved considerably since its onset; moderate dyspnea, palpitation, and morning headaches. Physical examination showed pallor, emaciation, and evidence of an old right hemiplegia. The lungs were normal. The heart was slightly enlarged. There was a loud blowing systolic murmur over the mitral area. Serial blood cultures taken on admission showed hemolytic streptococci which developed in culture only after seven days. There was a moderate microcytic, hypochromic anemia. The white blood cells numbered 6,700 per cubic millimeter. The urine contained a small number of erythrocytes and leukocytes.

Between May 27 and June 8, 1944, 700,000 units of penicillin was given intramuscularly. Two days after receiving the first injection of penicillin the temperature was normal and there was spectacular symptomatic improvement. However, on June 21 she suddenly developed generalized tonic and clonic convulsions lasting for two hours, followed by confusion. She became comatose on June 23 and died on June 26.

The anatomic findings at necropsy were extensive spontaneous subarachnoid hemorrhage of the base of the brain secondary to a large hemorrhage of the pons, almost healed endocarditis of the mitral valve (hemolytic streptococci, clinical), small recent infarct of the left lung, ancient infarct of the spleen and cystitis of the urinary bladder.

The changes on the mitral valve were mild—only slight toughening—but the changes in the brain were extensive. A thin layer of hemorrhage in the subarachnoid area covered the medulla, pons, cerebral peduncles, and portions of the cerebellum and temporal lobes. The pons contained an oval area of hemorrhage 2.5 cm. in diameter, and there was a perforation into the third ventricle. Both lateral ventricles and the third ventricle contained blood clot.

CASE 2.—Mrs. O. B., white, aged 22, five months pregnant, entered St. Joseph Hospital on May 12, 1944, complaining of a profuse vaginal discharge and dysuria for one month, chills, fever and multiple painful swollen joints for six days. The heart, lungs and abdomen were normal. Cervical and urethral smears and cultures showed gonococci. The patient was given a total of 24 Gm. of sulfamerazine in five days and was dis-

From the Departments of Medicine, Northwestern University and St. Joseph Hospital.

charged on May 17, symptom free. One week later at home the patient had a recurrence of her symptoms and again received 20 Gm. of sulfamerazine.

On June 24 the patient entered the hospital complaining of chills, fever, malaise and a weight loss of 17 pounds (7.7 Kg.). Essential physical findings at this time were a seven months pregnancy; daily fever to levels as high as 104 F.; pallor; fine moist rales in both lung bases; moderate enlargement of the heart; loud blowing systolic and diastolic murmurs at the left base, a harsh systolic murmur at the right base and a soft systolic murmur at the apex; and liver enlargement 4 cm. below the costal margin. The spleen was not palpated. There were no petechiae. There was a moderate hypochromic microcytic anemia. The white blood cell count was 17,600 cells per cubic millimeter. The urine contained many erythrocytes and leukocytes but no albumin or sugar. Serial blood cultures were negative after twenty-one days.

On June 27 the patient, in the seventh month of pregnancy, went into labor and delivered a viable baby. Intramuscular penicillin was then started, and in the next twelve days 1,200,000 units was given. During the first five days 1,100 mg. of heparin also was given. In addition the patient received transfusions

Fig. 1 (case 1).—A thin layer of hemorrhage in the subarachnoid area covers the medulla, pons, cerebral peduncles and portions of the cerebellum and temporal lobes. The pons contains an oval area of hemorrhage 2.5 cm. in diameter, with a perforation into the third ventricle. Both lateral ventricles and the third ventricle contain blood clot.

of whole blood. The temperature gradually subsided and reached normal in seven days. However, the patient developed an intractable cough, and there were many coarse rales scattered throughout both lung fields. The respiratory rate and pulse rate increased. The abdomen gradually became distended, and on July 7 there was a generalized anasarca. There was no abdominal pain or vomiting. The patient developed anuria on July 9 and died on July 10.

The anatomic findings at necropsy were vegetative and ulcerative endocarditis of the aortic and tricuspid valves with erosion and perforation of both valves; acute perforated ulcer of the stomach with extensive hemorrhage into both the lesser and greater peritoneal cavities; extensive petechial hemorrhages of the peritoneum, pericardium, pleurae and serosa of the small intestine; pronounced dilatation of the right atrium; slight dilatation of the left ventricle, right ventricle and left atrium; retained placenta in an enlarged uterus; acute splenic tumor; cloudy swelling of all viscera; chronic passive hyperemia of the liver, and bilateral hypostatic pneumonia.

The greater peritoneal cavity contained air and over 1 liter of partially clotted blood. The lesser peritoneal cavity was also filled with clotted blood. High up on the posterior wall of the stomach was an oval perforation 1 cm. in diameter.

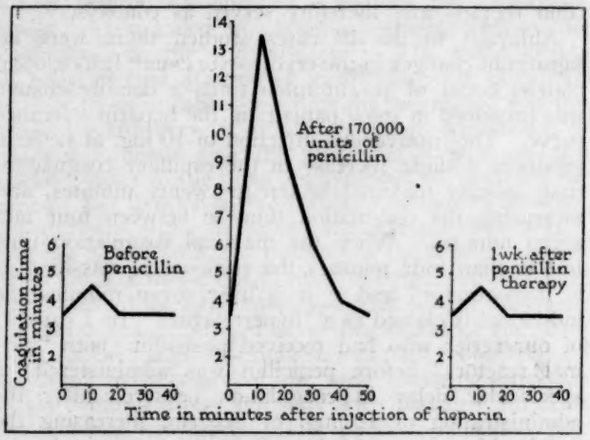

Coagulation time in minutes
Before penicillin
After 170,000 units of penicillin
1 wk. after penicillin therapy
Time in minutes after injection of heparin

Fig. 2 (Miss S.).—Interlobar empyema.

Adjacent to the perforation there was a small zone of superficial ulceration. The wall at this site was not thickened. The serosa of the small intestine and the mesentery were mottled with large petechial hemorrhages. Similar but less extensive hemorrhages were observed in the pericardium and pleurae.

COMMENT

The 2 patients whose histories are recorded present the following points of similarity: proved bacterial endocarditis, early improvement by penicillin therapy and fatal termination from hemorrhage, 1 by extensive cerebral hemorrhage, the other by widespread, intraperitoneal, mesenteric and pleural hemorrhages. One patient received heparin, while the other did not. Although one might consider the hemorrhage in each patient to be only a manifestation of the sepsis, we felt that there was enough evidence to warrant a study of the effect of penicillin on the clotting mechanism, and particularly to study the effect of penicillin on the reaction of the blood to heparin. This is particularly important, because many clinicians use heparin in con-

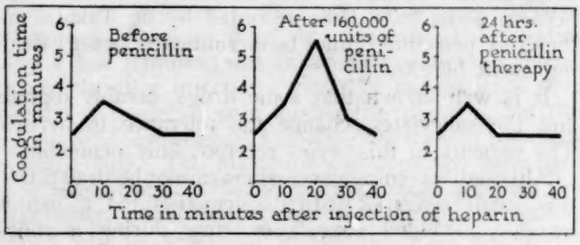

Coagulation time in minutes
Before penicillin
After 160,000 units of penicillin
24 hrs. after penicillin therapy
Time in minutes after injection of heparin

Fig. 3 (Mrs. S.).—Hodgkin's disease (control).

junction with penicillin in the treatment of bacterial endocarditis.

Studies were made on a series of patients before penicillin was administered, during the course of penicillin therapy and after the penicillin had been discontinued. These included erythrocyte counts, hemoglobin determinations (Sahli), prothrombin times (Quick), platelet counts (Rees and Ecker) and heparin tolerance

curves (de Takats).[1] In each case the penicillin was administered intramuscularly in doses of 10,000 Oxford units every three hours. The total dosage of penicillin employed varied from 140,000 to 2,500,000 units. In the patients studied there was a variety of disease conditions present. One half of the patients studied had diseases which are not considered suitable for penicillin therapy and therefore served as controls.

Although in the 10 cases studied there were no significant changes in the erythrocyte count, hemoglobin, platelet count or prothrombin time, a definite change was produced in some patients in the heparin tolerance curve. The intravenous injection of 10 mg. of heparin produces a slight increase in the capillary coagulation time, usually maximal in ten to twenty minutes, and increasing the coagulation time to between four and seven minutes. When the maximal coagulation time is less than four minutes the response is classified as a "hyporeactor" and if it is over seven minutes the individual is classed as a "hyperreactor." In 2 patients of our series who had received penicillin (both "normal reactors" before penicillin was administered) a spectacular delay in coagulation occurred after the administration of 10 mg. of heparin, increasing the maximal response to heparin to seven minutes in 1 patient, and to thirteen and one-half minutes in another. In 5 cases mild increases of one to two minutes were noted, but these were not considered

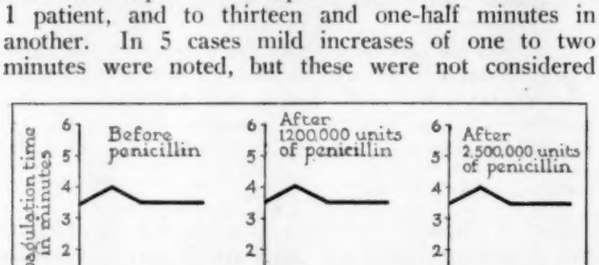

Coagulation time in minutes
Before penicillin
After 1200,000 units of penicillin
After 2,500,000 units of penicillin
0 10 20 30 40
Time in minutes after injection of heparin

Fig. 4 (Mr. M.).—Subacute bacterial endocarditis.

sufficiently high to justify any conclusion. In 3 cases no change occurred. Examples of the different types of response are shown in figures 2, 3 and 4.

Symptomatic reactions of an allergic type developed in 2 patients. Alarming dyspnea, cyanosis, cough, tachycardia, sweating and weakness were produced by the heparin injected while a course of penicillin was being given. Similar severe reactions from intravenous heparin alone have been recorded by de Takats, and therefore penicillin cannot be incriminated as the offending agent here.

It is well known that some drugs, notably digitalis and the salicylates, change the tolerance to heparin. The patients in this series received only penicillin.

Although sweeping conclusions cannot be drawn from this small series, 2 patients demonstrated a definite increase in blood coagulation time during a course of penicillin, as measured by the heparin tolerance test. Minor changes in 50 per cent suggest a slight tendency of a similar nature in others. This tendency seems to be particularly important in the treatment of patients with bacterial endocarditis if heparin is used, as an adjuvant to penicillin. These studies suggest that it is advisable to run heparin tolerance or heparin sensitivity tests as a precautionary measure if heparin and penicillin are to be used at the same time.

1. de Takats, G.: Surg., Gynec. & Obst. **77**: 31-39 (July) 1943.

SUMMARY

Death from extensive visceral hemorrhages occurred in 2 patients who had received penicillin therapy for bacterial endocarditis, in spite of great symptomatic improvement following the initial doses of the drug, and in spite of almost complete healing of the endocarditis in 1 case. Subsequent studies on 10 patients receiving penicillin showed profound effects on the sensitivity to heparin in 2 patients, no effect on the heparin tolerance curve in 3 patients and slight but inconclusive increase in 5 patients. No change in the hemoglobin, erythrocyte counts, platelet counts or prothrombin times was demonstrated.

2100 Burling Street, Chicago 14.

INTRA-ARTERIAL INJECTION OF PENICILLIN FOR INFECTIONS OF THE EXTREMITIES

PRELIMINARY REPORT

S. THOMAS GLASSER, M.D.
JOHN HERRLIN JR., M.D.
AND
BORIS POLLOCK, M.D.
NEW YORK

This report includes 24 cases treated for serious infections in the extremities. We present what we believe to be the first series in which penicillin was administered by the intra-arterial route. The excellent results obtained are noteworthy. These findings assume added importance at this time because 70 per cent of war casualties are associated with wounds in the extremities. An even higher percentage of traumatic lesions of the extremities are observed in war industries. Since these injuries are frequently complicated by infection, a preliminary report on the utilization of penicillin by the arterial route would seem to be timely.

HISTORY

The history of intra-arterial therapy dates back to 1914. In this year Goyanes [1] in Spain, Fiolle [2] in France and Heddaus [3] in Germany injected various drugs with more or less doubtful effect. A few years later, following the discovery of mercurochrome, occasional optimistic reports appeared in the literature. Dos Santos [4] and Lamas [5] in Portugal and Leriche,[6] de Fourmestrau [7] and Fredet [8] in France deserve credit for stimulating renewed interest in the intra-arterial method. The arterial route was utilized for the injection of mercurochrome, gentian violet, colloidal silver, acriflavine and other drugs and serums. Luccarelli [9] reported 36 cases in which the local pathologic con-

From the New York Medical College, Flower-Fifth Avenue Hospital and Metropolitan Hospital, Dr. Louis René Kaufman, Director of Surgery.

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2. Fiolle, Jean, and Fiolle, Paul: Essais d'hématose artificielle et d'angeio thérapie artérielle, Marseille méd. **16**: 597, 1914.
3. Heddaus, A.: Beiträge zur Heilserumbehandlung des Tetanus, München. med. Wchnschr. **61**: 2186, 1914.
4. Dos Santos, Reynaldo: Arterial Injections with Stasis in the Therapy of Infections, Surgery **5**: 436-443, 1939.
5. Lamas, A.: Thérapeutique par voie artérielle, Cong. franç. de chir. **42**: 384, 1933.
6. Leriche, R.: A propos de la thérapeutique des infectiones par voie intra-artérielle, Mém. Acad. de chir. **66**: 47, 1940.
7. De Fourmestrau, J.: La voie artérielle dans le traitement du tétanos, Mém. Acad. de chir. **63**: 550, 1937.
8. Fredet, M.: Les injections intraartérielles de mercurochrome dans le traitement des infections de membres des plaies atones et des ulcères variqueux, Cong. franç. de chir. **46**: 543, 1937.
9. Luccarelli, Vincenzo: Intra-Arterial Injection Therapy in Severe Disorders of the Extremities, Policlinico (sez. prat.) **45**: 1985 (Oct. 31); 2038 (Nov. 7) 1938.

dition was favorably influenced in every case from the point of view of control of the infection. Many of his cases which ordinarily would have required incision and drainage were cured by only one intra-arterial injection. He observed that, "no doubt, the intra-arterially injected gentian violet causes changes in the local circulation, witnessed by the purple coloration of the parts most seriously injured, as well as sensations of heat followed by relief of pain and a sense of comfort in the affected limb." Recently the sulfonamides have been used with excellent results. In the present war the Russian authors A. and E. Titelbaum,[10] reported their results as "striking" in which 100 to 150 cc. of 0.85 per cent solution of sulfanilamide was used in 15 cases. Other Russian surgeons, especially Martinoff,[11] mention the prophylactic value of mercurochrome and sulfanilamide for extremity wounds during the present war. In these cases débridement of wounds was routine.

PHYSIOLOGIC CONSIDERATIONS

The physiologic basis of the intra-arterial method is directed toward local concentration of the therapeutic agent into the infected tissues. The standard methods of applying antibacterial drugs are oral, intravenous, intramuscular and topical. In addition, penicillin is also being administered intrathecally, intrathoracically and intra-articularly with excellent results, these methods proving the efficacy of direct or local concentration. On the other hand, topical application must be differentiated from what we have termed "direct" or "local" use by virtue of the proved data that the former is effective only superficially. The beneficial effects observed when penicillin is deposited in pleural or synovial cavities is unlike the usual local application on wounded surfaces probably because penetration of the drug takes place more readily in the former method. Herrell, Nichols and Heilman[12] have shown that the greatest blood concentration of penicillin, until now, has been obtained by the intravenous route. However, we have been able to reach higher blood levels by means of the arterial method. It is obvious that any drug introduced by any of the preceding routes except the arterial must necessarily be diluted by the volume of the circulating blood. On the other hand, the intra-arterial method implies a minimal dilution of the medicament whereby a higher concentration than by any other means results in the tissues nourished by the artery utilized for the injection. Furthermore, in the presence of inflammation the capillary permeability increases, thus allowing for greater filtration of the drug, which is deposited in greater concentration in the locus of infection and subsequently is released slowly to the general circulation. The fixation of the drug in the infected area is even more effective if, immediately following an intra-arterial injection, a tourniquet is applied proximally for ten minutes. By the method of stasis the concentration of the drug increases. Dos Santos[4] showed by arteriographic studies that the application of elastic compression retarded the passage of medicaments into the general circulation. He injected sodium iodide into the brachial artery and applied a tourniquet proximally. Fluoroscopy revealed that about fifteen minutes after the injection the shadow was visible; then the vessel gradually lost its opacity, "but the tissue gradually became more accentuated, obviously due to the fixation of sodium iodide in the tissue." Other experiments which illustrated the phenomenon of concentration were those of Leriche[6] and Goyanes,[1] who obtained anesthesia of an extremity following the injection of procaine into the vein and artery respectively only by employing the method of stasis. They failed to obtain anesthesia without the application of the pressure cuff. The toxic effects of procaine and absence of anesthesia were evidenced only in those instances in which the tourniquet was not applied. However, it is also of great importance to know beforehand that the molecular weight, p_H and transfusibility of the drug is physiologically adapted for contact and fixation in the involved tissues. Following intra-arterial injection the vasomotor response, increased warmth of the limb and flushing of the skin are noted. How much of this is due to reactive hyperemia following the release of the tourniquet, and what part of this vasodilatation can be attributed to the action of the drug itself has not been determined. Leriche[6] observed an increased temperature of the limb following injection of the femoral artery not only with procaine but with antibacterial substances. His patients indicated that during the injection a wave of warmth descended along the injected artery. Besides the concentrated and prolonged action of antibacterial substances by the arterial route, this procedure allows for greater mobilization of the immunologic forces of the body against bacterial invasion.

COMPLICATIONS

The employment of drugs approaching isotonic concentration for intra-arterial injection should obviate serious complications. Lami[13] notes that there should be no hesitancy about injection through an artery, since it is less fragile than a vein; because elasticity of the needle puncture in the artery wall closes more rapidly than in a vein. Huet and Bargeton[14] and Wilmoth[15] established by animal experimentation that solutions injected intra-arterially were safest when isotonic and with a p_H near that of the blood, thereby avoiding damage to the intima. In our experience we have never encountered arterial thrombosis. Only few serious complications are recorded in the literature and these apparently due to faulty technic or poor selection of the medicament. Dos Santos[4] mentions occasional arterial and venous spasm in the upper extremity, rarely in the lower extremity. He has eliminated this complication after its occurrence by sympathetic ganglion block with procaine. He has never seen arterial thrombosis resulting from this method. Pain, lasting only a few minutes, was occasionally observed during or shortly after injection. Some of our patients complained of moderate pain during the injection, but this disappeared immediately following deflation of the blood pressure cuff. The literature also mentions hematoma as a complication. In no instance have we had this experience, probably because of attention to technic which will be described in the following paragraph. Leriche[6] has not experienced toxic reactions when using the arterial route for the introduction of mercurochrome which were noted when the intravenous route was employed. In our series of 24 cases reported in this paper, no complications except for occasional moderate transitory pain were found.

10. Titelbaum, A., and Titelbaum, E.: Intra-Arterial Introduction of Drugs for Treatment of Local Inflammatory Processes of the Extremities, Khirurgia **5-6**: 22, 1943.
11. Martinoff, D.: Intra-Arterial Injection of Antiseptic Drugs, Khirurgia **2-3**: 17, 1943.
12. Herrell, W. E.; Nichols, D. R., and Heilman, D. H.: Penicillin: Its Usefulness, Limitations, Diffusions and Detection, with Analysis of 150 Cases in Which It Was Employed, J. A. M. A. **125**: 1003 (Aug. 12) 1944.
13. Lami, G.: Direct Injection of Drugs into the Arteries, Paris, Thesis, 1937.
14. Huet, P., and Bargeton, D.: Sur quelques effets des injection intraartérielle, Presse méd. **44**: 677, 1936.
15. Wilmoth, P.: Treatment by Intra-Arterial Injection, Presse méd. **47**: 1249, 1939.

CONTRAINDICATIONS

Luccarelli [9] states that the intra-arterial method is contraindicated in hypotension, diabetes, nephritis and arterial incompetence, although he gives no justification for these beliefs. On the contrary, our experience leads us to disagree with this author's views. We have not found any contraindications in the intra-arterial method of utilizing penicillin. Arterial thrombosis as a disease entity might be considered as a possible hazard. We feel that it is of no significance other than that it would not lend itself to the introduction of the drug. Here the method of injecting the vein followed by stasis could be substituted. Furthermore, we have injected the femoral artery in the presence of advanced arteriosclerosis without any side-effects. Locally infected areas or thrombophlebitis may be considered as contraindications.

TECHNIC

We mention precautionary measures to be observed before outlining our technic of intra-arterial injection. We are in agreement with Wilmoth in cautioning against transfixion of the artery with the needle. This may be avoided by entering the artery obliquely. It is not essential that the needle be placed in the direction of the blood stream, as mentioned by many writers. Rhythmic jets of blood into the syringe must be observed before injecting. Our technic of intra-arterial injection is as follows:

We employ a 20 cc. syringe to which a gage 20 needle 2½ inches long is attached. In the lower extremity the injection is made into the femoral artery, piercing the skin in the crease of the groin. The left hand palpates the femoral artery, which is best felt above the inguinal crease, especially in obese persons. The artery is fixed between the index and third fingers of the left hand, and the needle is directed from below upward. Close proximity to the artery is noted when an arterial impulse is transmitted from the point of the needle to the syringe. A bright or light colored pulsating stream of blood appearing in the syringe, which contains 50,000 units of penicillin (10 cc.), indicates that the needle is within the lumen of the artery. In the upper extremity, depending on the location of the infection, the brachial artery is punctured at the elbow or more proximally. The blood pressure cuff, which has been applied proximal to the infected area at the beginning of this procedure, is inflated rapidly immediately following completion of the injection, which has been given at the rate of 1 cc. per second. The pressure in the cuff should be 280 to 300 mm. of mercury and is maintained for ten minutes. In order to avoid the possibility of hematoma formation, digital pressure over the puncture site is applied immediately on withdrawal of the needle.

Depending on the local effects and the systemic response (decrease in pulse rate and temperature), a second, third or even fourth intra-arterial injection may be necessary.

PENICILLIN DOSAGE AND EVALUATION

We have empirically used a dosage of 50,000 units of penicillin per injection in all of our cases. Although the clinical results were beyond expectations, the optimum minimal dosage is still left to be ascertained. In our series of cases reported in this paper we have dissolved 50,000 Oxford units of penicillin in 10 cc. of isotonic solution of sodium chloride. This may be regarded as being ideal for intra-arterial injection, since it is practically isotonic. The p_H of this solution as determined in our laboratories is 7.4 (p_H of blood is 7.3-7.5).

The bacterial flora commonly found in infections of the extremities is usually responsive to penicillin. The question arises how this drug of choice should be utilized to its best advantage. Romansky and Rittman [16] have described a new method for prolonging the action of penicillin by the medium of beeswax in peanut oil given intramuscularly. Fleming and his collaborators [17] in a recent paper mention the use of penicillin either by continuous administration with a low level for an extended period or by an intermittent method of high blood levels of penicillin for short periods. In the latter method the blood level is low before the succeeding injection is given. In most of our cases we found that a lapse of several days between injections did not alter the efficiency of our regimen, provided a careful clinical supervision was practiced, the status of the case being evaluated from day to day. This intermittent injection method was found to be advantageous by Bigger [18] in his experimental studies on the action of penicillin in vitro. He was prompted to conduct this investigation in seeking the cause for the not infrequent failures of penicillin action against staphylococci. He concluded that penicillin is bactericidal for Staphylococcus pyogenes in concentrations from 1/24 to 1 unit per cubic centimeter. In the serums of patients undergoing treatment, the concentrations are more commonly 1/16, 1/8 and 1/4 unit per cubic centimeter, while 1/2 to 1 unit occurs only occasionally. Furthermore, failure to sterilize broth containing Staphylococcus pyogenes is due to the survival of a small number of staphylococci called "persisters." It is believed that persisters are insensitive to penicillin because they are temporarily in a nondividing phase and because penicillin destroys only bacteria which are about to divide. Unlike resistant strains, descendants of persisters are readily destroyed by penicillin. Bigger [18] is of the opinion that there is good clinical evidence that many bacteria other than Streptococcus pyogenes and penicillin sensitive nonhemolytic streptococci also produce the same kind of "persisters." He concludes from his studies with staphylococci that the same might apply to other bacteria and suggests the use of the fractional or intermittent method of sterilization as employed to kill spores in culture mediums. During treatment all cocci in a susceptible phase should be killed by penicillin. During periods of absence of treatment, persisters should begin to divide and thereby become susceptible to penicillin. But, since the persister phase may be of long duration, several alterations of treatment would be required for the complete elimination of staphylococci from the body. Furthermore, it is desirable to maintain 1/2 to 1 unit per cubic centimeter for optimum effect. The wastefulness and impracticability of continuous intramuscular or intravenous injections of penicillin for long periods in the treatment of local infections in the extremities is apparent from the foregoing discussion. For these reasons the intra-arterial introduction of penicillin is ideal. The method is both local and economical. In our experience, one daily injection of 50,000 units of penicillin was sufficient to cope with even the severest infection. We have found concentrations as high as

16. Romansky, M. J., and Rittman, G. E.: A Method of Prolonging the Action of Penicillin, Science **100**: 196 (Sept. 1) 1944.
17. Fleming, A.; Young, M.; Suchet, J., and Rowe, A.: Penicillin Content of Blood Serum After Various Doses of Penicillin, Lancet **2**: 621 (Nov. 11) 1944.
18. Bigger, J. W.: Treatment of Staphylococcal Infections with Penicillin by Intermittent Sterilization, Lancet **2**: 497 (Oct. 14) 1944.

4.4 units per cubic centimeter of serum in venous blood taken eleven minutes following release of the cuff and 3.6 units in twenty-five minutes.

WAR WOUNDS: SUGGESTED APPLICATION OF INTRA-ARTERIAL METHOD

Our experience with the intra-arterial injection of penicillin, especially in cases of severe infections complicated by diabetes and arteriosclerosis, prompts us to suggest the use of this method for war wounds. We believe that many lives and limbs could be saved by the utilization of the arterial route. Experiences of this war have shown that, under the unfavorable or limited conditions near the battle fronts, even with the application of sulfonamide drugs and débridement primary wound closure is a risky procedure. At present the medical corps practices primary closure only for wounds of the head, face and chest, while in extremity wounds débridement without sutures is the accepted procedure. Occasionally secondary closure is performed. Wilson and Threadgill[19] report about 105 cases in which secondary closure of wounds was practiced in order to obtain "better cosmetic results, more rapid general improvement, and the avoidance of the possibility of protracted ulceration of a large cicatrix."

The following scheme of treatment of war wounds is suggested:

1. *Prevention of Infection.*—(*a*) The first intra-arterial injection of penicillin should be given as soon as possible. This simple procedure might be allotted to an advanced medical unit equipped with a sterile 20 cc. syringe, needle and penicillin. Wherever possible, débridement should precede the injection.

(*b*) If débridement is deferred, a second intra-arterial injection following this procedure is advisable because the initial injection will not have destroyed the bacteria in the contaminated necrotic tissue which is deprived of its normal blood supply.

(*c*) In some cases with minimal contamination and damage of the tissues a primary wound closure followed by intra-arterial injection could tentatively be attempted with or without débridement.

(*d*) Treatment of war wounds of the extremities by intra-arterial penicillin will unquestionably increase the number of cases suitable for early secondary closure and for skin grafting because fewer patients will develop infection. A secondary wound closure should be followed by an additional injection.

2. *Treatment of Infected Wounds of the Extremities.*—(*a*) Infected war wounds of the extremities should receive an intra-arterial injection of penicillin preceded by careful débridement and all pus pockets laid wide open. The number of penicillin injections will depend on the gravity of the case, so that supplementary injections should be given at intervals—every one, two or more days.

REPORT OF CASES

CASE 1.—D. K., a white woman aged 67, was admitted with the diagnosis of impending diabetic gangrene of the left foot complicated by infection. The left foot was much swollen and presented two draining sinuses, one between the first and second toes and another midway down the plantar surface. There were definite signs of cellulitis on the dorsum. The temperature was 101 F. On Sept. 16 and 17, 1944 50,000 units of penicillin was given intra-arterially with considerable improvement. On the 19th an incision was made extending from the sinuses between the toes down to the sinus on the plantar surface. This was deepened to the subcutaneous tissues, which were excised and included necrotic and sloughing tendons and muscle, although no actual pus was visible. An additional incision was made on the dorsum of the foot beginning between the great toe and the second toe and extending for a distance of 2 inches. Necrotic tissue was removed. Petrolatum gauze was used for packing and 50,000 units of penicillin given intra-arterially. Bacteriologic examination of the smear showed Staphylococcus aureus, Streptococcus viridans and Escherichia coli. The temperature returned to normal postoperatively and the diabetic status was greatly improved. The wound remained clean and granulating except near the region of the heel on the plantar surface, which showed some necrosis. X-rays revealed osteomyelitis of the third, fourth and fifth metatarsal heads and corresponding toes. On October 2 extensive débridement (fig. 1) was performed including excision of involved bone and necrotic tendons and fascia on the plantar surface followed by 50,000 units of penicillin intra-arterially. This was repeated October 9 and November 7 and 20. The postoperative course was excellent. Healthy granulations appeared and the temperature remained normal. However, with the realization that the foot would be nonfunctioning even if complete healing resulted, it was deemed advisable to amputate below the knee. This operation was performed and followed by 50,000 units of penicillin intra-arterially. Healing occurred by primary union.

This patient was admitted with what is generally agreed on as a definite indication for emergency amputation because of pronounced arteriosclerosis with diabetes complicated by spreading infection on both the dorsum

Fig. 1.—Debridement in case 1.

and plantar surfaces of the foot. The usual expected course without amputation would be a rapid spread of the gangrenous process and infection proximally up the leg with systemic reaction. In this case response to intra-arterial penicillin was almost immediate: relief of pain, return of temperature to normal and definite improvement in the diabetic status. Because of inadequate débridement and drainage (this being our first case) a second débridement was necessary before complete control was obtained. Unfortunately the gangrenous process had already destroyed a great portion of the foot, thereby leaving a limb which would be unsuitable for prosthesis. The amputation below the knee was elective. Primary healing of the sutured stump in the presence of infection is definitely attributed to the use of penicillin. This case demonstrated to us the absolute necessity for thorough débridement and drainage in the presence of necrosis and encapsulated pus, since it is agreed that penicillin will not act in such mediums.

CASE 2.—J. V., a woman aged 65, a Puerto Rican with diabetic arteriosclerotic gangrene of the second, third, fourth and fifth toes with osteomyelitis of the heads of the third, fourth and fifth metatarsal bones (fig. 2), had a purulent discharge and inguinal adenopathy; the temperature was 100 F. Smear showed Staphylococcus aureus. Penicillin 50,000 units was administered intra-arterially, repeated two days later with

19. Wilson, H., and Threadgill, F. D.: Secondary Suture of War Wounds, Bull. U. S. Army M. Dept., 1944, no. 82, p. 77.

extensive débridement, including amputation of the second to fifth toes and the corresponding metatarsal heads with excision of soft tissues. A third penicillin injection was given six days later. The wound immediately became clean and started to granulate within a few days.

Excellent results were obtained in a diabetic patient with suppurative gangrene. This type of case would

Fig. 2.—Appearance of foot in case 2.

ordinarily require emergency amputation through the thigh.

Case 3.—A. S., a white woman aged 41, was in diabetic coma. There was moist gangrene of the left fourth toe with extension of infection into the plantar spaces. Emergency care was given for the coma. Intra-arterial penicillin 50,000 units on two consecutive days resulted in decided improvement. On the fourth day the injection was repeated and the involved toe was amputated, with débridement on the plantar surface. A smear showed Staphylococcus aureus and Streptococcus viridans. The postoperative course was good, but impaired circulation of the fifth toe required additional amputation, including the metatarsal head (fig. 3). Rapid recovery with complete diabetic control resulted. The wound filled in with scar tissue and the patient was able to walk.

In this case diabetic coma with spreading infection of the foot and gangrene of the toe was completely controlled by débridement and intra-arterial penicillin, resulting in a foot suitable for ambulation.

Case 4.—F. H., a white woman aged 56, had diabetic arteriosclerotic gangrene of the left foot including the second, third, fourth and fifth toes; osteomyelitis; cellulitis, and lymphangitis of the dorsum. Three doses of intra-arterial penicillin (50,000 units) were given, the first on the day of admission, the second on the following day when débridement of the left foot with amputation of the second and third toes extending into the intermetacarpal spaces was performed, and the third four days later. A smear showed Staphylococcus aureus. Complete control of the diabetic ketosis with granulation followed. The history revealed that sulfonamide drugs had been taken without avail before admission to the hospital.

In this case serious infection in the foot of a diabetic patient associated with gangrene of the toes responded rapidly to arterial penicillin therapy.

Case 5.—T. H., a Negro man aged 32, was suffering from a human bite on the dorsal surface of the left middle finger of five days' duration. The finger was diffusely swollen and accompanied by slight pain at the onset, which became progressively worse and on admission presented lymphangitis and axillary lymphadenitis associated with a temperature of 101.4 F. Intra-arterial penicillin 50,000 units was given, and drainage with excision of a small amount of slough was performed. The temperature was normal on the following day. Penicillin was repeated in forty-eight hours. The wound remained clean and the patient was discharged.

The usual difficulties encountered in human bites are due to the mixture of organisms in this type of wound. Ordinarily response to treatment is refractory, but with intra-arterial penicillin complete control resulted.

Case 6.—N. W., a Negro woman aged 63, had early diabetic gangrene of the second and fourth toes of the left foot. There were infected ulcers on the second, third, fourth and fifth toes, with osteomyelitis of the phalanges, cellulitis spreading into the plantar spaces, advanced arteriosclerosis and pronounced diabetes. Intra-arterial penicillin 50,000 units was given and disarticulation of the second to fifth toes performed; an elliptic incision included most of the ball of the foot, and the underlying soft tissues were excised. A smear showed Staphylococcus aureus and Escherichia coli. Penicillin was repeated on the second, fourth and tenth days. The postoperative course was excellent and granulations appeared within five days, filling in the wound completely within ten days.

This is similar to the first case except that a more complete removal of necrotic tissues at the onset proved more efficient.

Case 7.—M. N., a white woman aged 55, had a perforating ulcer on the plantar surface of the left foot, diabetes, persistent pain for the previous seven months, a moderately purulent

Fig. 3.—Foot in case 3 after amputations.

discharge, the margins being covered by hard callus, and moderate arteriosclerosis. Excision of the ulcer and surrounding callus with intra-arterial penicillin 50,000 units was performed. The injection was repeated two days later. Infection was completely controlled and granulations were evidenced within one week. The patient was discharged completely healed two weeks later.

In the presence of arteriosclerosis with diabetes, an ulcer of the mal perforans type is nearly always refractive to treatment. The response to intra-arterial penicillin was exceptionally good.

CASE 8.—D. F., a white woman aged 65, with arteriosclerosis and an infected gangrenous ulcer on the second toe of the right foot with lymphangitis extending on the dorsum, complained of persistent pain. Intra-arterial penicillin 50,000 units was injected and repeated on the third day. Infection was completely controlled, leaving a clean ulcer. Pain was greatly relieved following the first injection.

This case is one of advanced arteriosclerosis complicated by lymphangitis. The danger of progressive moist gangrene in this type of case is recognized. To get results within twenty-four hours is extraordinary.

CASE 9.—E. G., a white woman aged 43, suffered from very large painful infected varicose ulcers on the left leg. A bilateral saphenous vein ligation had been performed five weeks before admission. Intra-arterial penicillin 50,000 units was given and repeated on the third day. Pain was completely relieved within twenty-four hours following the first injection. The ulcer appeared clean on the fourth day.

In spite of bed rest and recent vein ligation, infection of the varicose ulcer persisted until penicillin was given. The organisms found on initial smear were Staphylococcus aureus and streptococci.

CASE 10.—C. P., a Negro woman aged 27, with chronic gonorrheal pelvic inflammatory disease had tenosynovitis of the index finger with much swelling for the past five days, probably of gonococcic origin. Brachial intra-arterial penicillin 50,000 units was given and repeated in forty-eight hours. Immediate improvement was noted, with almost complete subsidence of pain. The patient was discharged two weeks later, completely cured, without limitation of movement of the finger.

This case of probable gonorrheal tenosynovitis readily responded to intra-arterial penicillin without surgical treatment.

CASE 11.—M. G., a white woman aged 56, whose left leg had been amputated through the thigh one month before admission, had diabetic arteriosclerotic gangrene, with infection of the right big toe. Intra-arterial penicillin 50,000 units and amputation of the big toe with the head of the metatarsal was performed and the injection repeated forty-eight hours later (fig. 4). The patient was discharged completely healed three weeks later. The original smear showed Staphylococcus aureus, Escherichia coli and Streptococcus viridans.

This case presents rapid healing, immediate clearing up of infection and rapid epithelization in a case of arteriosclerosis and diabetes complicated by infection.

CASE 12.—Z. A., a white man aged 57, had diabetic arteriosclerosis with cellulitis and lymphangitis on the dorsum of the right foot with much edema. Intra-arterial penicillin 50,000 units was given on admission and resulted in localization of the infection within twenty-four hours. The second injection with incision and drainage was performed forty-eight hours later and resulted in a clean healing wound. The smear showed Staphylococcus aureus.

The dreaded complication of infection in diabetic arteriosclerosis was completely localized in twenty-four hours and cleared up on the third day following a second dose of penicillin.

CASE 13.—D. F., a white man aged 68, had arteriosclerotic gangrene of the right middle toe with localized infection. Intra-arterial penicillin 50,000 units was administered and amputation of the toe was performed. Postoperatively the wound remained clean and granulated.

One injection of penicillin intra-arterially served to keep the wound clean and allowed granulation in spite of advanced arteriosclerosis.

CASE 14.—I. N., a white woman aged 68, had diabetic arteriosclerosis, with gangrene of all the toes of the right foot and moist gangrene of the entire plantar surface and distal part of the dorsum. The involved area was completely debrided and intra-arterial penicillin 50,000 units was given. The injection was repeated for the next four consecutive days. A smear showed gram positive cocci and diplococci and gram positive bacilli. The diabetic status was completely controlled within twenty-four hours. Insulin was not required and the temperature returned to normal. The patient was discharged with a healthy granulating wound.

Fig. 4.—Foot in case 11 after amputation of toe.

The use of penicillin intra-arterially apparently assumes complete control of infection, so that surgical local procedures may be performed which would ordinarily be contraindicated.

CASE 15.—M. J., a white man aged 75, had moist gangrene of the left foot, arteriosclerosis, lymphangitis extending half way up the leg, a temperature of 102 F. and generalized toxicity. A low thigh amputation was performed and the stump was closed without drainage immediately followed by intra-arterial penicillin 50,000 units, which was repeated daily for three injections. The stump healed in one week by primary union.

This case presents the extraordinary result of healing by primary union in an amputation stump closed without drainage in the presence of lymphangitis.

CASE 16.—M. D., a white man aged 52 with diabetes, presented arteriosclerosis, diabetic polyneuritis, hypertension and gangrene of the fourth right toe with spreading cellulitis extending to the dorsum of the foot. His temperature was 103.2 F. The involved toe was amputated and intra-arterial penicillin 50,000 units was given. The temperature subsided within twenty-four hours and penicillin was repeated the following day. However, in spite of the absence of infection the gangrene spread because of arterial insufficiency. The patient refused amputation. Three weeks later in the presence of advanced gangrene and spreading lymphangitis extending up the leg a low thigh amputation was performed with primary closure and resulted in healing by primary union.

In spite of pronounced infection and lymphangitis, primary closure of the stump is possible with the aid of intra-arterial penicillin.

CASE 17.—B. S., a white man aged 70, had necrotic ulcers of the right foot, arteriosclerosis, diabetes and infection. Intra-arterial penicillin 50,000 units was given and repeated four days later. Improvement was prompt and granulations appeared at the ulcer sites within one week. A smear originally showed Staphylococcus aureus.

Acute necrosis and ulceration in the presence of arterial insufficiency complicated by diabetes in a patient 70 years of age is always regarded with alarm. Penicillin prevented extension of infection and we are impressed by the rate of healing which, although delayed by arteriosclerosis, is nevertheless far more rapid than we have ever observed under any other method of treatment.

CASE 18.—P. B., a white man aged 74, was obese and had diabetic arteriosclerotic gangrene of the second toe and heel with infection. Intra-arterial penicillin 50,000 units was given and repeated four days later, resulting in complete control of the infection.

This is another example in which infection was completely controlled in the presence of pronounced arterial incompetence in a diabetic patient.

CASE 19.—N. Y., a white man aged 43, was suffering from dorsal subaponeurotic space infection of the left hand with lymphangitis and pronounced edema. Penicillin 50,000 units was injected into the brachial artery, and incision and drainage were performed. The smear showed Streptococcus viridans and aerobic and anaerobic gram positive diplococci in chains. Injections were repeated on the second and fourth days. Postoperatively the infection subsided completely within twenty-four hours.

The efficacy of intra-arterial penicillin is shown in a case of serious hand infection due to a mixture of virulent bacteria.

CASE 20.—J. O., a white man aged 42, had tenosynovitis of the index finger of the left hand with cellulitis. A bilateral incision followed by intrabrachial injection of penicillin 50,000 units was performed. A smear showed Staphylococcus aureus. The injection was repeated in twenty-four and seventy-two hours with complete control of the infection.

Rapid subsidence of infection in a case of tenosynovitis was obtained with the use of penicillin by the intra-arterial method.

CASE 21.—M. A., a Negro woman aged 39, had ulnar and radial bursitis of the right hand; her temperature was 102.2 F. Two injections of penicillin 50,000 units were given into the brachial artery within forty-eight hours. The swelling on the dorsum and the pain and limitation of movement of the fingers cleared up after three days without surgery.

In the presence of a serious infection without suppuration or necrosis, intra-arterial penicillin will control the infection and result in a cure without surgery.

CASE 22.—C. S., a white woman aged 47 with diabetes, arteriosclerosis and gas infection of the great and second toes extending into the plantar spaces, was given intra-arterial penicillin 50,000 units, and incision and drainage were performed. The injection was repeated on the second and fourth days. The smear showed aerobic Staphylococcus aureus, Escherichia coli and anaerobic Staphylococcus aureus. Complete control of the infection was evident within forty-eight hours.

A severe mixed infection with gas formers in the presence of arteriosclerosis and diabetes was readily controlled by the intra-arterial method.

CASE 23.—F. S., a white woman aged 65 with diabetes, arteriosclerosis and cellulitis of the dorsum of the right foot, was given one intra-arterial injection of penicillin 50,000 units, with complete control of the infection.

This case is another example of the excellent response to the intra-arterial method under adverse conditions.

CASE 24.—J. H., a white man aged 76, had an infected hematoma of the middle of the left leg with cellulitis, lymphangitis and inguinal adenitis. Intra-arterial penicillin 50,000 units was given. The following morning drainage was spontaneous. The injection was repeated and the infection completely controlled.

Intra-arterial penicillin assumed complete control of an infected hematoma despite the presence of suppuration. This result is only partly due to the spontaneous drainage.

COMMENT

These 24 case reports illustrate the excellent results obtained with the use of intra-arterial penicillin, especially in the severe intractable types of infection. Emphasis is placed on infection occurring in extremities as a complication of arteriosclerosis with or without diabetes. It is generally agreed that in cases of arterial insufficiency the primary objects in treatment are, first, to improve the collateral circulation and, second, to prevent infection, which in the greater percentage of cases is the precursor of moist gangrene. Tissues with poor blood supply are exceedingly vulnerable to infection. As previously mentioned, the intra-arterial method with stasis resulted in favorable vasomotor reactions when the circulation was not greatly impaired. Whether or not this side effect is attributable to reactive hyperemia is to be determined. Another noteworthy observation which deserves attention is that, in the absence of suppuration or necrosis, a single injection usually suffices for definite improvement or cure. It may be argued that the usual intermittent intramuscular injection of penicillin might also give good results. But certainly one can predict favorable results without reservation when the intra-arterial route is utilized because local concentration is most efficacious. The relief of pain is another outstanding result. Many patients have definitely been saved from major amputation. Again, a lower amputation site has become permissible because infection can be controlled. Primary closure of all amputation stumps in the presence of infection is now practiced in our surgical service. The value of this innovation is obvious. It is expected that subsequent studies will reveal a wider scope for the application of the method of intra-arterial injection with penicillin and stasis because of the high local concentration of the drug used by the intermittent method. Included in our technic is débridement of necrotic and devitalized tissues or incision and drainage in the presence of suppuration, performed prior to arterial injection. This is important because pus cavities and dead tissue are not reached by this or any other method of administering antibactericidal drugs. We realize that this preliminary report is incomplete from the standpoint of thorough investigation and research. Determinations of local tissue and systemic circulation concentrations of penicillin should be made in every case. These data are contemplated for subsequent publication.

SUMMARY

1. Twenty-four cases of severe infections of the extremities were successfully treated by the intra-arterial injection of penicillin.

2. The intra-arterial route allows for greater local concentration of penicillin.

3. Relief of pain is observed.

4. Amputation may be obviated in many cases.

5. Lower amputation sites are more frequently permissible.

6. Primary closure of the stump in the presence of infection is successful.

7. One injection may effect a cure in the presence of inflammation without suppuration or necrosis.

8. The method is economical and rapid in its effect.

1049 Park Avenue.

Clinical Notes, Suggestions and New Instruments

PRELIMINARY OBSERVATIONS OF THE GASTRIC MUCOSA IN PATIENTS WITH INFECTIOUS HEPATITIS

CAPTAIN WILLIAM A. KNIGHT AND
LIEUTENANT ROBERT C. COGSWELL
MEDICAL CORPS, ARMY OF THE UNITED STATES

In view of the prominence of anorexia, nausea, vomiting and upper abdominal pain in the clinical picture of infectious hepatitis, and because of the paucity of information concerning the pathology of this disease, it was deemed advisable to make observations with the gastroscope to determine whether abnormalities might be found which would throw light on the pathogenesis, symptomatology and pathology of this condition. Patients with infectious hepatitis were therefore examined with the aid of the Schindler flexible gastroscope on the day following admission, except in 1 instance as noted. This report concerns 9 patients whose gastrointestinal symptoms were limited to their present illness. The clinical picture and laboratory findings of these patients were in complete accord with the diagnosis of infectious hepatitis. In every case the history indicated that the disease had been naturally transmitted and was not related to any preceding parenteral injection.

In 7 of the patients examined, the appearance of the mucosa was found to deviate from the normal, and in 2 no abnormality was noted. One of the 2 with normally appearing mucosa had noticed jaundice four days prior to admission, and the other had yellow scleras one month before coming to the hospital. Of the 7 patients whose mucosa was considered to be abnormal in appearance, the clinical course or picture of 1 patient was different from that noted in the other 6. This patient was admitted with epigastric pain, nausea, belching, sour eructations, anorexia and constipation, present to a moderate degree for approximately two weeks before admission and was examined twenty-five days after admission while free from icterus. The examination revealed findings which are generally interpreted as indicating superficial gastritis, i. e. bright, velvety appearing mucosa, with hyperemia, edema, increased highlights and adherent mucus involving the antral and distal fundic portions of the stomach. There were no ulcerations visible. He was discharged from the hospital and readmitted approximately two weeks later with a history that jaundice appeared the day of discharge and seven days after the first gastroscopy. He was reexamined on two occasions during the second admission while he was actually icteric, and a normal appearing gastric mucosa was observed. The remaining 6 patients were all examined with the gastroscope for the first time between four and nine days after the onset of clinical icterus.

In those cases in which deviations from the normal appearance of the gastric mucosa were observed, the area involved was always the antral portion of the stomach, and in some instances the abnormal appearing area extended into the fundus. The findings which have impressed us as being most distinctly abnormal gave the appearance through the gastroscope of being almost identical with small aphthous ulcers commonly seen in the mouth. Five patients in this series were observed to have these ulcerations. The lesions were small, apparently 2 to 5 mm. in diameter, shallow, ovoid or round, with a dirty white base, and in some instances were surrounded by a narrow red areola. They were found in the antrum and on the angularis and varied in number in a given patient from one to four. In 2 patients flakes of mucus were observed adherent to the mucosa of the antral region. Hyperemia and mucosal texture characteristic of superficial gastritis and the ulcerations coexisted in 4 of the aforementioned cases. In none of these patients was peristalsis apparently impaired.

Further study is essential before any conclusions can be formulated with regard to the relationship between the findings in the gastric mucosa which we have noted and infectious hepatitis. The lesion, in our opinion, may ultimately prove to be due to localization of a virus infection and may be either early or late manifestations of the disease or to be secondary to some physiologic disturbance resulting from infection with the virus of infectious hepatitis. On the other hand, the lesion may prove to have only an accidental relationship to infectious hepatitis and will not be found with regularity in cases of this disorder which are examined in the future.

Further cases are to be studied, and a more comprehensive report will be submitted subsequently.

From the Regional Hospital, Fort Benning, Georgia.

THE TETRALOGY OF FALLOT

REPORT OF AN UNUSUAL CASE

EDWARD W. MISKALL, M.D., EAST LIVERPOOL, OHIO

The tetralogy of Fallot,[1] consisting of pulmonary stenosis, right ventricular hypertrophy, interventricular septal defect and dextroposition of the aorta, is the most common combination of congenital cardiac defects attended by cyanosis.

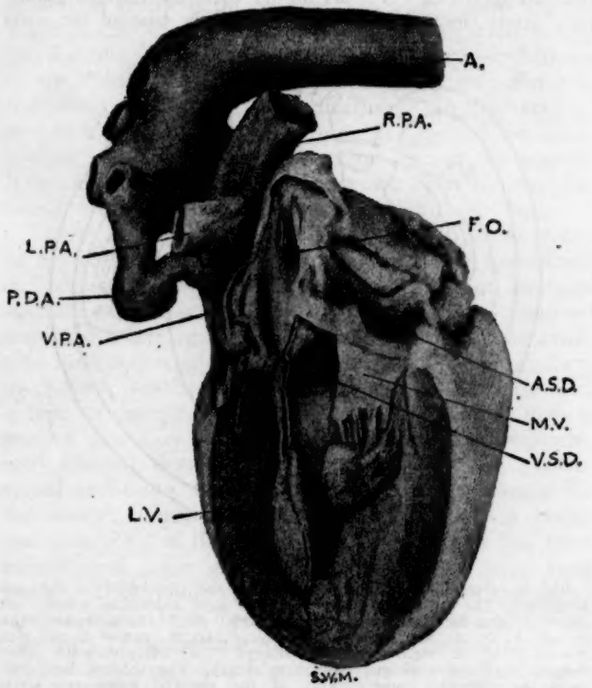

Fig. 1.—Appearance of the heart in the case presented. Part of the wall of the left auricle and left ventricle has been removed. The mitral valve has been divided longitudinally and the anterior flap reflected to expose the interventricular septal defect. *A*, aorta; *A. S. D.*, auricular septal defect; *F. O.*, foramen ovale; *L. P. A.*, left pulmonary artery; *L. V.*, left ventricle; *M. V.*, mitral valve; *P. D. A.*, patent ductus arteriosus; *R. P. A.*, right pulmonary artery; *V. P. A.*, vestigial pulmonary artery; *V. S. D.*, ventricular septal defect.

This case is presented because it had, in addition to the classic features of the tetralogy, an interauricular septal defect, a functional foramen ovale and a widely patent ductus arteriosus. The coronary venous sinus was received by the left auricle. There was no innominate artery. The right subclavian and the right common carotid arteries arose directly from the aortic arch.

REPORT OF CASE

B. A. P., a white girl aged 2½ years, seen July 23, 1944, had been cyanotic since birth. Clubbing of the fingers and toes was first noted at the end of the first year. Growth and development had been retarded. The birth weight was 7 pounds

1. Fallot, A.: Contribution à l'anatomie pathologique de la maladie bleue (cyanose cardiaque), Marseille-med. **25**: 77, 138, 207, 270, 341 and 403, 1888.

11 ounces (3,487 Gm.). Fretfulness and dyspnea had been present since birth. There had been no acute infections, but there had been sudden attacks of increased dyspnea and cyanosis. These attacks came on without apparent cause at varying intervals. They lasted fifteen minutes to an hour and subsided spontaneously. There were no convulsions or syncope.

Physical examination showed considerable generalized cyanosis, with clubbing of the fingers and toes. A loud coarse systolic murmur was heard over the precordium, maximal at the base of the heart. A soft high-pitched early diastolic murmur was heard over the same area, but it did not fill diastole. No x-ray examination of the chest could be secured. An electrocardiogram showed extreme right axis deviation. Neither the liver nor the spleen was palpable.

The attacks of dyspnea increased in frequency and severity. The death of the patient occurred Oct. 12, 1944 in a particularly severe seizure that came on during a relatively mild upper respiratory infection.

The autopsy was limited to the chest. The lungs were moderately congested. The heart, which was globular, weighed 88 Gm. with the aortic arch attached (normal weight 45 to 55 Gm.). It contained two large auricles and two hypertrophied ventricles. A short fibrous cord, the vestigial pulmonary artery, located just to the left of the base of the aorta

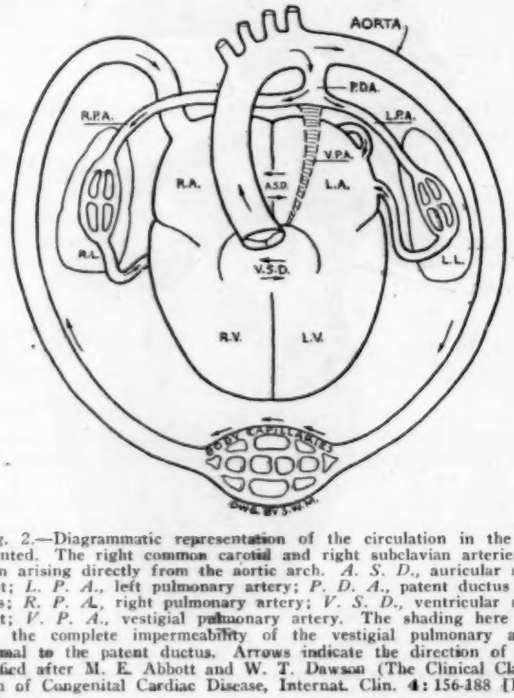

Fig. 2.—Diagrammatic representation of the circulation in the case presented. The right common carotid and right subclavian arteries are shown arising directly from the aortic arch. *A. S. D.*, auricular septal defect; *L. P. A.*, left pulmonary artery; *P. D. A.*, patent ductus arteriosus; *R. P. A.*, right pulmonary artery; *V. S. D.*, ventricular septal defect; *V. P. A.*, vestigial pulmonary artery. The shading here indicates the complete impermeability of the vestigial pulmonary artery proximal to the patent ductus. Arrows indicate the direction of flow. Modified after M. E. Abbott and W. T. Dawson (The Clinical Classification of Congenital Cardiac Disease, Internat. Clin. **4**: 156-188 [Dec.] 1924).

(fig. 1), was proximally impermeable but expanded distally to meet the widely patent ductus arteriosus. From the latter, the right and left pulmonary artery branches arose. The right auricle received the superior and inferior venae cavae. The left auricle received the pulmonary veins and the coronary venous sinus. There was a rather large (and probably functional) patent foramen ovale. Posteroinferior to the foramen ovale was an interauricular septal defect 1 cm. in diameter. The auriculoventricular valves were normal. There was a large interventricular septal defect in the membranous portion of the septum which measured 9 to 10 mm. across. The aorta was dextroposed, overriding the defect, so that two thirds or more of the aortic cross section was on the right ventricular side and one third or less on the left ventricular side. The aortic cusps were normal. The coronary arteries were normal and arose in the usual location. The left and right ventricular walls each averaged 10 mm. in thickness. In the upper anterior aspect of the right ventricular wall was a roughly funnel-shaped cavity with its apex pointing to the left and upward. It was 12 mm. in length and 5 to 6 mm. in diameter at its ventricular orifice. This was apparently the vestigial pulmonary infundibulum.

COMMENT

Although this classic tetrad of congenital cardiac defects bears the name of Fallot,[1] who first completely analyzed and recognized it as a clinical entity in 1888, it had first been described by Sandifort[2] in 1777. Hope[3] (1842) also described several cases.

Congenital pulmonary stenosis may follow on a fetal endomyocarditis or it may result from developmental defects. White[4] is of the opinion that the pulmonary valve and infundibulum show evidence of fetal endocarditis more frequently than other parts of the heart because the chief burden of the fetal circulatory effort is theirs. If this occurs late, i. e. after the septums have closed, it may be the sole defect; more often, however, other defects are present, particularly those of the interventricular septum. In Abbott's[5] 1,000 cases of congenital heart disease there were 150 cases of pulmonary stenosis or atresia of the pulmonary infundibulum or valve, 35 cases of aortic or subaortic stenosis or atresia, 19 cases of tricuspid stenosis or atresia and 11 cases of mitral stenosis or atresia.

The developmental type of pulmonary stenosis results, according to Harris and Farber,[6] from delayed involution of the bulbus cordis and from failure of the interventricular septum to close completely. The aorta is frequently dextroposed in these cases, so that it overrides the septal defect and thus receives blood from both ventricles. Furthermore, disturbances in the normal process of torsion may produce the most bizarre anomalies.

Failure of a physiologic mechanism, rather than an embryologic malformation, is given by Kennedy and Clark[7] as the explanation of isolated patency of the ductus arteriosus. However, in this case the patent ductus arteriosus is obviously a compensatory mechanism for the much more serious tetralogy of Fallot.

The patent foramen ovale, while of sufficient size to be functional, was doubtless unimportant as compared to the large auricular septal defect (primitive ostium primum) located posteroinferior to the foramen ovale. In Abbott's[5] series of 1,000 congenital cardiovascular defects there were 36 interauricular septal defects due to persistence of the ostium primum. Eighteen of them complicated other defects, as in the case presented herewith. This type of defect adds to the work of the right auricle and ventricle by pouring an extra volume of blood into the right auricle through the septal defect. This direction of flow from left to right, Uhley[8] ascribes to the effect of gravity, since, as he points out, the right auricle lies below the left, the septum lying horizontally.

The altered cardiodynamics are shown in figure 2. The patent ductus arteriosus provides that some of the blood from the aorta reaches the right and left pulmonary arteries. The extra work imposed on the right side of the heart by the increased blood volume can be appreciated. The right auricle receives blood from the venae cavae and from the left auricle through the interauricular septal defect. The right ventricle must pump the blood it receives from the right auricle against the extra head of pressure that is present in the pulmonary circuit as the result of the patent ductus. The latter, however, may not be as great as is ordinarily present because of the already inadequate amount of pulmonary blood.

Little Building.

2. Sandifort, E.: Observationes anatomico-pathologicae, Lugd. Bat., P. v. d. Eyk et D. Vygh, 1777, cap. 1, fig. 1.

3. Hope, J.: A Treatise on the Diseases of the Heart and Great Vessels, Philadelphia, American ed. 1, from London ed. 3, Haswell and Johnson, 1842, pp. 449-460.

4. White, P. D.: Heart Disease, ed. 3, New York, Macmillan Company, 1944, p. 301.

5. Abbott, M. E.: Atlas of Congenital Cardiac Disease, New York, American Heart Association, 1936, chart I, pp. 60-61.

6. Harris, J. S., and Farber, S.: Transposition of the Great Cardiac Vessels with Special Reference to the Phylogenetic Theory of Spitzer, Arch. Path. **28**: 427-502 (Oct.) 1939.

7. Kennedy, J. A., and Clark, S. L.: Observations on the Physiological Reactions of the Ductus Arteriosus, Am. J. Physiol. **136**: 140-147 (March) 1942.

8. Uhley, M. H.: Lutembacher's Syndrome and a New Concept of the Dynamics of Interatrial Septal Defects, Am. Heart J. **24**: 315-328 (Sept.) 1942.

COUNCIL ON PHARMACY AND CHEMISTRY

SECRETARY'S INTRODUCTION

For many years the Council on Pharmacy and Chemistry has considered claims for therapeutic usefulness offered on behalf of drugs sold to the medical profession and the general population for the prevention and treatment of infections of the feet. Frequently there was lacking adequate scientific evidence to support the claims. Almost equally lacking, unfortunately, were adequate standards for judging the actual comparative merits of such preparations. At its October 1942 meeting the Council proposed that several authorities in this field be invited to prepare a report on the status of fungicidal agents and offer criteria to aid in the evaluation of such preparations. The Council already has published criteria concerning antibacterial compounds (THE JOURNAL, *Feb. 20, 1943, p. 593). Dr. Fred D. Weidman, Dr. Chester W. Emmons, Dr. Joseph G. Hopkins and Dr. George M. Lewis accepted the Council's invitation and for the past two years have been carrying on investigations, the results of which are incorporated in the following report. The Council wishes to express its appreciation for the assistance provided by these investigators and has adopted their report for publication. This report is intended for all who are interested in the problem of treatment of infections of the feet and especially for medical practitioners, industrial surgeons and manufacturers interested in submitting preparations to the Council for inclusion in New and Nonofficial Remedies.*

AUSTIN SMITH, M.D., *Secretary.*

THE WAR AND DERMATOPHYTOSIS

WITH SPECIAL REFERENCE TO TREATMENT AND FUNGICIDE TESTING

FRED D. WEIDMAN, M.D.
Professor of Dermatologic Research, University of Pennsylvania School of Medicine
PHILADELPHIA

CHESTER W. EMMONS, PH.D.
Principal Mycologist, U. S. P. H. S., National Institute of Health
BETHESDA, MD.

JOSEPH G. HOPKINS, M.D.
Professor of Dermatology, Columbia University College of Physicians and Surgeons

AND

GEORGE M. LEWIS, M.D.
Associate Professor of Clinical Medicine (Dermatology), Cornell University Medical School
NEW YORK

When it appeared inevitable that the United States would be drawn into the European conflict, fresh significance at once accrued to dermatophytosis. War, marching soldiers and their feet are inseparable problems. True, dermatophytosis had already achieved a real position in the medical sun. A ubiquitous annoyance in all strata of society, it occasionally became incapacitating. Notable advance had been made in studies of its pathogenesis, and the principles of treatment, at least, had become crystallized. However, both the general public and the medical profession appeared to be content with the more or less desultory course of events in the study of dermatophytosis, as long as it did not lead to important general constitutional sequelae and remained essentially a disorder of our lowly toes and feet. Indeed, it was the secondary dermatophytids of the hands that aroused most concern; industrial compensation suits often hinged around the question of dermatophytosis or no dermatophytosis.

Following the discovery that no less than 8 per cent of all hospital admissions in the Army and Navy were for cutaneous disease and that dermatophytosis ranked second on the list, certain government agencies as well as the Council on Pharmacy and Chemistry of the American Medical Association supplied funds and facilities whereby its problems could be inquired into more accurately. Among other things this involved a reconsideration of the pathogenesis. To what extent are the predisposing causes of importance, and to what extent are the fungi the exciting agents? Is the reappearance of the disease, once it has cleared up, a recurrence of the infection or is it a reinfection? In the way of prophylaxis, should our energies be directed the more against the predisposing causes or against the specific fungi in the premises, and have we been overemphasizing fungicidal chemicals in treatment?

These questions have been largely unanswered because many clinical studies made in clinics and offices and directed toward their solution have not included suitable control series. When these questions assumed importance among the armed forces there became available men requiring treatment and in sufficient numbers to provide treated and control groups of adequate size, a type of discipline which made control and follow-up studies possible, a reasonably uniform environment, well trained dermatologists and mycologists, professional assistants, and facilities and funds adequate for the study. Under these favorable conditions a better understanding of dermatophytosis of the foot has been gained and some advances in its control have been made. This report can cover only a few of the many studies which have been made under these conditions. By way of indicating the wealth of material, Peck studied 2,123 individuals in industry, Keeney had access to 128 naval cadets or more, and Weidman and Glass employed 116 prisoners at a penitentiary.

ETIOLOGY

After it was shown that dermatophytes [1] were the cause of certain intertrigos of the toes, it was assumed by many physicians that they were the cause in all cases of this condition. It now appears certain that bacteria [2] may be the cause in some cases. Hopkins [3] was unable to demonstrate fungi even after repeated microscopic examinations in as many as 30 per cent of military personnel with lesions of the feet. He concluded that

Most of the section on fungicide testing is unpublished. It was conducted by a subcommittee of the American Public Health Association working at the National Institute of Health. Drs. C. M. Brewer, E. G. Klarmann and G. G. Slocum were members of this subcommittee, and Dr. C. W. Emmons was the fourth member. The National Institute of Health gave permission for the publication of the results in advance of its own reports.

1. The commonest species in the United States are: 1. Trichophyton interdigitale (synonyms Trichophyton gypseum, Trichophyton mentagrophytes, Kauffman-Wolff fungus). "Trichophyton interdigitale" has been selected for the purposes of this paper because it is the more widely employed name. 2. Trichophyton purpureum (synonyms Trichophyton rubrum, Epidermophyton rubrum and others). 3. Epidermophyton inguinale (synonym Epidermophyton floccosum). A complete statement of synonyms can be found in the Manual of Clinical Mycology by Conant and others, Philadelphia, W. B. Saunders Company, 1944.

2. Mitchell, J. H.: Streptococcic Infection Simulating Ringworm of the Hands and Feet, J. A. M. A. **104**: 1220 (April 6) 1935.

3. Hopkins, J. G.; Hillegas, A. B.; Camp, E.; Ledin, R. B., and Rebell, G.: Treatment and Prevention of Dermatophytosis and Related Conditions, Bull. U. S. Army M. Dept., June 1944, No. 77, p. 42.

some of these nonmycotic lesions were due to infection by Staphylococcus aureus or to sensitization to S. aureus, shoe polish, fungicides, antiseptics and similar sensitizing substances. Hypostasis due to long standing and trauma account for other groups of these disturbances of the feet. However, the extreme point of view of Benedek [4] that fungi are only secondary invaders not etiologically related to lesions of the feet is untenable in view of the many instances of experimental production of dermatophytosis.[5] The facts seem to be that fungi cause the majority of intertrigos of the toes but that bacteria and sensitization are responsible for a considerable number. Improper hygiene of the feet seems to be an important predisposing factor.[6] The too frequent acceptance of the diagnosis of dermatophytid of the hands has likewise given place to a recognition of the role of sensitization to nonmycotic agents in the majority of these cutaneous lesions.

Recurrence versus Reinfection.—This subject is still under lively discussion. Every physician is familiar with the apparent cures, followed by outbursts. The answer to the question naturally hinges on whether the causative fungi are eradicated in the apparently cured cases or still remain on the skin, quiescent but still viable. The evidence from the laboratory is contradictory. Some authors have cultured the fungi from apparently normal feet, while others were unable to do so. On one point all dermatologists are agreed, namely that fungi can remain for long periods within diseased nails without provoking an inflammatory reaction; the nails thus constitute an innocent looking reservoir. On the other hand, with the fungi so ubiquitous on man and viable for as long as 433 days in dry scales,[5] it appears logical that some reattacks must be due to reinfection: the environment harbors fungi.

It would be desirable to know the relative importance of recurrence and reinfection, but that information is not now available because of the difficulty of determining that treatment has actually eradicated the fungus from the skin. This cannot be proved by culture studies because there is a significant number of failures to isolate a fungus when it is known to be present and it is impossible to take an adequate sample for the detection of a remote and inapparent focus. The role of reinfection, on the other hand, cannot be disregarded because we cannot know certainly that the fungus has been removed from shoes, clothing, floors and the like.

One of us (G. M. L.) believes that the species of fungus concerned offers an answer. Thus, Epidermophyton inguinale infections are easily cured; therefore a second attack should be a reinfection. On the other hand, Trichophyton purpureum ones are so resistant to treatment that some of the fungi remain viable on the skin and accordingly a reattack would classify as a recurrence. In a case of infection with Trichophyton interdigitale it may be either way; the fungi may or may not remain on the skin, depending on the manner in which the patient has been treated. Thus, an active tissue response to treatment leads to the eradication of the fungus. In any event, studies by Hopkins and his associates [8] indicated that no reliance could be placed on attempts to prevent reinfection. Dermatophytosis flared up when hot weather, heavy shoes and violent exercise reactivated quiescent lesions on the patient's own feet. Obviously, prophylaxis of dermatophytosis should be a two pronged drive; first and foremost, to destroy completely the fungi on the skin and, second in importance, to destroy them in shoes and other environment. It is such a short step between shoes and pedal skin that the two must be handled together.

PROPHYLAXIS

Sterilization of Previously Worn Shoes.—Obviously, rather severe limitations are placed on the choice of sterilizing agents when dealing with leather. Theoretically, gases are preferable to liquids, but Greene [7] found that even formaldehyde vapor did not satisfactorily penetrate into the cracks of the shoes. Accordingly, he devised the following methods for mass sterilization and reconditioning as needed in institutions and military establishments where suitable apparatus was available. Immersion in 1 per cent formaldehyde solution for five minutes sterilizes the entire shoe. For supplementary mechanical cleansing the shoes were washed in a 0.3 per cent soap solution, followed by washing in water for two minutes. The last traces of formaldehyde can be neutralized in a two minute bath of 0.5 per cent sodium bisulfite, but this is probably unnecessary. Pliability was restored by a bath in a 10 per cent oil emulsion for two minutes; 0.5 pentachlorophenol was incorporated in it to prevent development of mold during drying of the shoes. As to the choice of oils, the National Oil Products Company's "Tanoyle No. 1052" (a "cationic oil" consisting of a mixture of polyethyleneoamines, fatty oil and mineral oil) was preferred. Neatsfoot oil was emulsified with a 2 per cent solution of Armour and Company's "A. M. Coco B acetate" (coconut oil fatty acid converted to its acetate salt) but needed agitation to maintain the emulsion.

For the sterilization of small numbers of shoes, the following method can be substituted:

1. Cleanse the shoes of any extraneous débris or dirt. Use any mild soap and water.
2. Dry as well as possible with a dry cloth.
3. Put in each shoe a pad of cotton; spread it out to make an insole.
4. Pour onto this insole (in each shoe) 1 teaspoon of solution of formaldehyde U. S. P. diluted 1 : 10.
5. Put the shoes in a paper box, close the lid and wrap in paper. Allow the shoes to remain in this box for at least six hours.
6. Remove them from the box, throw away the cotton and air the shoes for twenty-four hours.
7. Apply saddle or harness soap liberally to all parts of the shoes, inside and out. Allow this to dry.
8. Polish shoes as usual and wear.

Hygiene of the Feet.—The prophylactic value of foot baths is probably negligible. Early reports of their value may have failed to take into account the increased and beneficial attention to foot hygiene which may have been but incidental to education about the condition and to the use of the foot bath. There are three vulnerable points; viz., maintenance of the chemical at fungicidal concentration, the short period of exposure and enforcement of use. Sodium hyposulfite, sometimes used, is completely worthless in in vitro tests of fungicidal value, and sodium hypochlorite deteriorates rapidly. The period of exposure is too short to be of value, Bonar and Dreyer [8] having demonstrated that Trichophyton in

4. Benedek, T.: Critical Survey of the Mycological Literature of the Year 1938, Mycopathologia **2**: 281, 1940.
5. Weidman, F. D.: Laboratory Aspects of Dermatophytosis, Arch. Dermat. & Syph. **15**: 415 (April) 1927.
6. Sulzberger, M. B.; Baer, R. L., and Hecht, R.: Common Fungous Infections of the Feet and Groins, Arch. Dermat & Syph. **45**: 670 (April) 1942.
7. Greene, H. S.: Report on the Microbiological Flora and Sterilization of Used Shoes, J. Am. Leather Chem. A. **40**:96 (March) 1945.
8. Bonar, L., and Dreyer, A. D.: Studies on Ringworm Funguses with Reference to Public Health Problems, Am. J. Pub. Health **22**: 909 (Sept.) 1932.

epidermal scales is killed by sodium hypochlorite only after an exposure of an hour. Finally, enforcement of use is difficult because of the reasonable aversion of persons to walking through a common, sometimes filthy, foot bath.

One of the more newly developed fungicides, sodium propionate, may be employed in 1 per cent concentration in powdered talc.

TREATMENT

The general hygienic measures already indicated should accompany the active, fungicidal treatment. As to the latter, the most important single item is conservatism. Do not overtreat. Every dermatologist is familiar with the severe chemical dermatitides which his patients often exhibit at the first visit and which must be corrected before proceeding in the more or less conventional ways. Such "horrible examples" are the result of disregard of the long established dictum that acute dermatoses should be treated with the mildest types of local applications; stronger, stimulating ones should be reserved for lesions in a subacute or chronic stage.

Accordingly, the choice of fungicide will vary notably in dermatophytosis, depending on the location of the lesion and the form that the inflammation takes in the individual case. This, together with methods of application, is available in standard textbooks [9] and in the very recent report by Hopkins and his associates.[2] For the purpose of this communication, only the results of tests of new fungicides will be recorded.

The most promising of these is paralleled in the use of sodium or calcium propionate in bread dough and dairy products for the purpose of inhibiting the growth of molds; they are marketed under the trade name of "Mycoban." After Peck and Rosenfeld [10] had demonstrated that propionate inhibited human pathogenic fungi, Keeney and Broyles [11] found it effective against various forms of ringworm and in otomycosis, thrush and blacktongue. It is used in 10 per cent concentration, both powder and ointment. Ointment was used at night on toes and soles; in the morning it was removed and the powder was dusted on. Their tabulation indicates excellent results. Lately, Keeney and his co-workers [12] have reemphasized the value of propionate-propionic acid ointment as satisfying the qualifications, "enumerated in this report, of an ideal preparation for the treatment of tinea pedis." They were inclined to prefer it to undecylenate-undecylenic acid ointment. Moreover, in some respects it was as effective as penicillin against bacteria.

At a penitentiary, Weidman and Glass [13] compared six different forms of treatment on 116 prisoners. Whitfield's ointment, as well as 10 per cent boric acid in powdered talc, were included as standards of comparison, more or less, against four proprietary substances: Zephiran (a mixture of alkyl dimethyl-benzyl ammonium chlorides), Cresatin (metacresyl acetate), Pomeio (potassium mercuric iodide) and Iodolate (iodocholeate). Surprisingly, the boric acid powder was highly efficient. Cresatin was equally efficient, while Whitfield's ointment followed rather closely. The remaining three preparations were found unsuitable in their hands. These studies were conducted in the winter, when the lesions were relatively quiescent. They renew attention to the value of boric acid and place Cresatin on the list of fungicidal agents that are useful against dermatophytosis.

Effects of Sweat on Fungicidal Value of Chemicals.—This subject has not been investigated but should be checked in future studies, just as the role of serum in modifying the effectiveness of certain disinfectants and antiseptics is well known in the bacteriologic field. On the one hand, sweat is said to have fungicidal value of itself; [14] on the other hand, sweaty feet predispose to dermatophytosis. An unrelated consideration is the effect that it may have on the fungicide.

Similarly, the role of detergents which might be combined with fungicides and which are applied to the skin as simple mechanical cleansers will have to be established. They may be incompatible. Data in the bacteriologic field will be found in papers by Baker, Harrison and Miller.[15]

STANDARDS FOR IN VITRO FUNGICIDE TESTING

The subject of standards for in vitro fungicide testing was brought to a head by the war. Several methods of testing fungicides had been advanced prior to the emergency, but all were open to criticism. A serious attempt had not been made to resolve the various methods into a standard one such as the phenol coefficient for bacterial disinfectants and antiseptics is. It is obvious that conditions among the fungi are different. Special consideration must be given to (1) the kinds of fungous cells (such as conidia) that are to be employed as test objects, (2) the selection of the standard fungicide that will be reasonably representative of fungicides (iodine, benzoic acid) and (3) the choice between liquid or solid mediums. These problems in in vitro tests, although they have been approached, have not been solved in sufficient completeness and detail to permit the establishment of a universally useful, single, standard fungicidal test, but headway is being made. A systematic and searching attack is being made in the matter by a subcommittee of the American Public Health Association composed of C. M. Brewer, C. W. Emmons (chairman), J. G. Hopkins, E. G. Klarmann, G. G. Slocum and F. D. Weidman.

It is urgent that a standard test be established promptly. Thus, with the prospect of large sales to our several war departments, manufacturers have been and are still asking themselves whether their proprietary disinfectants and antiseptics have value also against fungi. On inquiry they find that there is not any fungicide test that has been accepted as standard and that the routine phenol coefficient test of the bacteriologist will not suffice. True, the Bureau of Ships made a praiseworthy attempt,[16] but it erred at least in selecting "Trichophyton rosaceum" as the test object. This point will be covered further in this review and has been corrected by the Bureau of Ships. Incidentally, the circular just cited may serve, pro tem, as a pattern or basis of consideration for fungicide testing in all its aspects.

9. The most comprehensive and well illustrated one in respect to dermatophytosis is Lewis, George M., and Hopper, Mary E.: An Introduction to Medical Mycology, ed. 2, Chicago, Year Book Publishers, 1943.

10. Peck, S. M., and Rosenfeld, H.: The Effects of Hydrogen Ion Concentration, Fatty Acids and Vitamin C on the Growth of Fungi, J. Invest. Dermat. **1**: 237 (Aug.) 1938.

11. Keeney, E. L., and Broyles, E. N.: Sodium Propionate in the Treatment of Superficial Fungous Infections, Bull. Johns Hopkins Hosp. **73**: 479 (Dec.) 1943.

12. Keeney, E. L.; Ajello, L.; Broyles, E. N., and Lankford, E.: Propionate and Undecylenate Ointments in the Treatment of Tinea Pedis and an In Vitro Comparison of Their Fungistatic and Antibacterial Effects with Other Ointments, Bull. Johns Hopkins Hosp. **75**: 417 (Dec.) 1944

13. Weidman, F. D., and Glass, F. A.: Arch. Dermat. & Syph., to be published.

14. Peck, S. M.; Rosenfeld, H.; Leifer, W., and Bierman, W.: Role of Sweat as a Fungicide, Arch. Dermat. & Syph. **39**: 126 (Jan.) 1939.

15. Baker, Z.; Harrison R. W., and Miller, B. F.: Action of Synthetic Detergents on the Metabolism of Bacteria, J. Exper. Med. **73**: 249 (Feb.) 1941; The Bactericidal Action of Synthetic Detergents, ibid. **74**: 611 (Dec.) 1941; Inhibition by Phospholipids of the Action of Synthetic Detergents on Bacteria, ibid. **74**: 621 (Dec.) 1941.

16. Dec. 15, 1942, circular 51D6 (Int), paragraph F-2b.

The subject of methods was brought down to 1939 by Burlingame and Reddish.[17] These authors contended for the employment of solid medium and of five different species of fungi as test objects instead of one. Incidentally, they too erred in including "Trichophyton rosaceum" in the test. They criticized Emmons's[18] method (a modification of the phenol coefficient method) because, among other things, it employed liquid mediums. There can be no question that their technic is difficult in view of the necessity of handling many small pieces of agar. It seems also that their technic would be unreliable in the differentiation of fungicidal and fungistatic action on account of the difficulty of thoroughly washing the fungicide from the test block of agar. The contention that the ease and extent of penetration of the agar block by the fungicide is an indication of the ability of the fungicide to penetrate such a material as epidermis seems unfounded.

Shortly thereafter, Klarmann, Shternov and Costigan[19] proposed a modification of the phenol coefficient method in which "Tr. rosaceum" was again erroneously recommended as the test organism. The spore suspension was prepared by culturing the fungus on broth containing glass beads, shaking the culture with the beads vigorously for thirteen minutes and suspending the conidia in the broth in which they grew, together with whatever metabolites and protoplasm from the broken fungous hyphae might be present. Obviously, both conidia and hyphal cells were here represented as test objects.

A critical comparison of the various methods of fungicide testing, made by the subcommittee of the American Public Health Association already mentioned, revealed faults in them and attempts were made to set up a more dependable method. The committee concluded that technics similar to those of the phenol coefficient test, modified according to the necessities imposed by the use of a fungus as a test organism, seemed to be best adapted to evaluation of water soluble and water miscible fungicides. (The problem of testing non-water soluble products presents even greater difficulties.[20]) It emphasized the importance of adherence to certain principles and the recognition of the limitations of their methods as follows:

1. The test organism should be a pathogenic fungus etiologically related to dermatophytosis of the foot. The so-called "Trichophyton rosaceum" widely used in fungicide testing is a common saprophytic soil fungus, Fusarium, not related to dermatophytosis.[21]

2. The test fungus must be handled and conserved carefully in order to prevent contamination as well as its degeneration and deterioration with respect to sporulation and phenol resistance. Stock cultures must be tested at suitable periods in respect to these factors.

3. Conidia of approximately uniform size, free of hyphal elements and culture medium, should be suspended in isotonic solution of sodium chloride and this suspension should be exposed at a uniform temperature for measured intervals to the fungicide dilutions.

4. It must be clearly recognized that this is an in vitro test and that a relative advantage of one fungicide as revealed by the test is not necessarily reflected in greater therapeutic efficiency. Conidia are used as test material not because they are supposed to be like the parasitic growth phase of the fungus but because they are relatively uniform and can be readily obtained in large numbers; i. e., for practical reasons. Naturally or artificially infected skin scales, hairs or wool can be used as test material in research studies, but it is doubtful that they are suitable for the routine testing of fungicides by a standard method because of the difficulty of obtaining sufficiently large numbers of uniform pieces.

The test is frankly an in vitro test such as is appropriate in testing the action of fungicides on floors and the like, and attempts to read more into it is ill advised. The therapeutic value of products to be examined may be a more important consideration, by and large, than their mere fungicidal action, but this should be tested by methods individually designed to answer the specific questions posed. Unfortunately, attempts to arrive at a compromise test in which, for example, the inherent fungicidal activity of a drug, its toxicity or irritant properties and its ability to penetrate keratin shall be measured in one procedure do not hold much promise. Laboratory tests must be designed to measure one of these characteristics at a time.

EVALUATION OF FUNGICIDES FOR CLINICAL USE (IN DERMATOPHYTOSIS)

As in the case of fungicide testing for disinfectant purposes, the following pattern is submitted only as an interim one; i. e., until improvements are made. They are much needed in respect to toxicity tests. Much additional work must be done before a reasonably watertight method is established. It will be noted that, naturally, it parallels the method for testing disinfectants and antiseptics as recommended by the Council on Pharmacy and Chemistry of the American Medical Association.[22] It is divisible into three parts: (1) laboratory tests of the fungicide, (2) clinical tests and (3) toxicity tests.

1. *In Vitro Tests of Fungicide.*—The phenol coefficient test for disinfectants and antiseptics as modified by the American Public Health Association subcommittee should be used. For the convenience of workers, this is resubmitted, but in synoptic form. A detailed report will be published in the *American Journal of Public Health* for 1945 of the Standard Methods Committee for the Examination of Germicides and Antibacterial Agents.

(*a*) The test fungus should be Trichophyton interdigitale. A suitable strain, No. 9533, is procurable from the American Type Culture Collection, Georgetown University, 3900 Reservoir Road, Washington, D. C. It should survive ten minutes' exposure at 20 C. to phenol 1:60 but not to a strength of 1:45.

(*b*) Spore suspensions of this test fungus should be prepared from ten day agar cultures in a concentration of 5 million conidia per cubic centimeter. For performing the test, 0.5 cc. of this suspension is added to 5 cc. of the fungicide concentration being tested.

(*c*) Samples for viability tests should be taken at five, ten and fifteen minute intervals and planted in a

17. Burlingame, E. M., and Reddish, G. F.: Laboratory Methods for Testing Fungicides Used in the Treatment of Epidermophytosis, J. Lab. & Clin. Med. **24**: 765 (April) 1939.

18. Emmons, C. W.: Fungicidal Action of Some Common Disinfectants on Two Dermatophytes, Arch. Dermat. & Syph. **28**: 15 (July) 1923.

19. Klarmann, E. G.; Shternov, V. A., and Costigan, S. M.: A Method For the Evaluation of Water Soluble and Water Miscible Fungicides Used in the Prevention of the Spread of "Athletes' Foot," J. Bact. **42**: 225 (Aug.) 1941.

20. Hillegas, A. B., and Camp, E. D.: Testing of Fungicides Insoluble in Water, J. Invest. Dermat., to be published. Acetone and propylene glycol are substituted as solvents because they are not fungicidal. The authors used the cylinder (penicup)-plate method such as is used in testing penicillin-like substances; any agar plate method introduces a factor of penetration of the fungicide which is highly undesirable. The *p*u was found to be highly important in influencing the power of a fungicide. Undecylenic acid had high fungistatic value.

21. Emmons, C. W.: Misuse of the Name "Trichophyton Rosaceum" for a Saprophytic Fusarium, J. Bact. **47**: 107 (Jan.) 1944.

22. Criteria for Evaluation of Skin Disinfectants, J. A. M. A. **121**: 593 (Feb. 20) 1943.

liquid medium containing 1 per cent Difco Neopeptone and 2 per cent chemically pure dextrose, p_H 5.6-5.8. A liquid medium is essential for the rapid dissipation of the fungicide carried over. In the case of fungicides exerting a strong fungistatic effect, subcultures must be made.

(*d*) The so-called "Trichophyton rosaceum" should not be used as a test species. It is less resistant than Trichophyton when tested by the method outlined here, although it often appears to be more resistant in plate tests.

The test procedures follow the plan outlined in United States Department of Agriculture Circular 198 for the determination of phenol coefficients.

2. *Clinical Tests and Their Evaluation.*—This subject will be discussed in some detail both because it is paramount in importance and because it is the most difficult phase of fungicide testing. It is fundamental that any opinions on this point should be based on planned studies and not on the general impressions which depend more or less on the memory of the investigator. This involves the use of prepared preliminary outlines and of a protocol for each patient. In proper, fully critical planning, the following criteria should be adhered to; in addition, certain sources of error will be pointed out:

(*a*) Selection and Grading of Patients: The number of patients should be sufficiently large to permit their division into a test group and a control group. Each of these, in turn, should be large enough to permit results that will be significant when later divided into subgroups for purposes of analysis. In consultation, a group of dermatologists has estimated 50 as the minimum number for both the test and the control group. Bed patients are not suitable, because dermatophytosis sometimes disappears spontaneously with bed rest.

Each of the two groups should contain an equitable representation of mild, moderate and severe cases. To this end it is advantageous to indicate on a diagram on the protocol just what the extent and type of lesion are for each patient.

(*b*) The Environment: This and other circumstances should be comparable in the two groups. The groups should be tested simultaneously. Thus, results from group A which were secured in winter would not be comparable to ones secured on group B in the summer; dermatophytosis is worse in the summer. Similarly, results should be checked with age groupings in the two test groups lest it have too much of a disturbing influence in the evaluations. Youths are far more predisposed than the aged.

(*c*) Laboratory Diagnosis: As a check against the clinical diagnosis, scrapings should be examined under the microscope for the presence of fungus and also cultured at the beginning of the studies. These examinations should be regarded as only supplementary to the clinical findings; many cases of valid dermatophytosis fail to yield confirmatory laboratory evidence, but the laboratory examinations may clarify doubtful clinical cases, and a knowledge of the identity of the species may be valuable when analyzing therapeutic results later. Thus, a fungicide might be eventually discovered which was efficacious against Trichophyton purpureum or other fungus but not against other species, and vice versa.

(*d*) Number and Duration of Treatments: As a working rule, applications should be made night and morning for two weeks. A final or subfinal examination should be made at the end of four weeks.

(*e*) Faithfulness of Patient to Treatment: Since it involves the human element, this is perhaps the most treacherous aspect of the entire evaluation and is one that can quite upset results. The investigator should appraise the human type of each patient before admitting him to the test series and have no hesitance in rejecting the unpromising ones. During the course of the tests, diplomatic questioning of the patient, together with observation of the lesions for traces of the medicament, should be practiced after the manner of the detective. Lapses in treatment demand that the patient be removed from the series and is one more reason for securing a larger number of patients at the beginning of the work than will be employed in the final evaluation.

(*f*) Privacy on Part of Patients: Patients should be requested not to discuss their treatment programs with other patients; they may influence one another's opinions. For obvious reasons, clinical tests should not be conducted on patients who are employed in plants which have a gainful interest in the fungicide being tested.

(*g*) Local Irritant Effect of Fungicide: This should be substantially nil, considering the number of fairly effective therapeutic agents now existent which are free from irritant effects. Certainly, the development of any reactions that are at all severe should at once condemn the agent.

(*h*) Sensitization to the Fungicide: This factor enters into and is routinely inquired for in tests of local applications in general. In the case of dermatophytosis it will largely take care of itself during the clinical tests of fungicidal value, where the applications are "interrupted" in the natural course of events. The appearance of flare-ups shortly after the eighth day of treatment should be watched for. If they do not appear, it may be taken for granted that the fungicide is not a sensitizer; if they do appear, a special set of tests for sensitization must be made.

(*k*) Toxic Systemic Effects: These should not play a role of importance in the treatment of dermatophytosis; there is scant likelihood of absorption from relatively restricted areas of skin. However, there is not any guaranty that the proposed fungicide will not be later recommended by a manufacturer as a general fungicide [23] or be self prescribed by the patient for an ailment which will permit absorption. Phenol compounds are in point. To be quite safe, animal tests should therefore be required save in exceptional circumstances, indicating whether the substance is toxic when administered internally and, if so, the amount that can be absorbed from skin. Such animal tests can follow the plans already developed for bacterial disinfectants and antiseptics. The Bureau of Ships Circular already cited, page 4, paragraph F.-2d may be followed in this connection.

(*l*) Readings of Results of Treatment: These should be made without any knowledge of the identity of the patient or of the treatment that has been employed; an assistant should have removed, if possible, any traces of telltale fungicide that may remain. Only in this way can the factor of bias be completely removed and a fair, impartial evaluation secured. If at all possible, the readings should be made by a disinterested person.

23. In fact, the Council on Pharmacy and Chemistry of the American Medical Association is opposed to advertising to the public of medicaments that might be used for self medication. The Council recognizes that certain agents such as vitamins and antiseptics may be used by the general population for prophylactic purposes but not for treatment (see New and Nonofficial Remedies 1944, pp., 16, 23 and 24).

(*m*) Mycologic Checks on Therapeutic Results: More than in the case of the laboratory examinations for purposes of diagnosis, these will have value only of a kind supplementary to the clinical opinions because of the increased difficulty in laboratory demonstration of fungi in treated lesions. At the conclusion of therapy they should be made on the "cured" and "nearly cured" patients and again on the cured patients four weeks after cure. Positive results will have larger definitive value because they will indicate that the fungicide has not killed; negative ones will have the same (and lesser) significance as under other circumstances, namely that there is still an outside chance that fungi are still present but not demonstrable. In any event this mycologic check should be performed if for no other reason than to have the data at hand when making final evaluations. They may turn the balance when wavering in a decision as to cure or no cure. The competence of the examiner in recognition of fungi is of paramount importance.

(*n*) Grading of Results: "Cured," "almost cured," "improved," "stationary" and "worse" are suggested, but each worker is at liberty to select any system that suits his purposes. All workers, though, should go on record to themselves beforehand for their own guidance as to the criteria that they should follow in grading; from this there should be no deviation later. A subdivision like this into five grades reduces the number of cases available for subsequent statistical purposes and illustrates once again the necessity for numerous patients to begin with. Opinions of patients as to results should not be depended on too much; in cases of doubt they should be discounted. Patients commonly regard themselves as cured when itching ceases. It will be conducive to accuracy if the physician has an assistant who will independently grade the results, the final grading being decided in consultation on the spot.

3. *Toxicity Tests.*—These should be performed depending on the individual circumstances surrounding the chemical concerned. Where there is a hazard the Bureau of Ships circular entitled "Disinfectant, Germicide and Fungicide," page 4, paragraph F.-2d should be followed. Ten healthy adult albino rats weighing between 150 and 250 Gm. should be employed, none pregnant. They should be fed as usual. Three-tenths cc. of the fungicide (standard strength) per kilogram of body weight should be slowly inserted obliquely into the peritoneal cavity. The animal should then be given the usual food and water and observed for untoward effects for seventy-two hours.

OTHER CONSIDERATIONS IN DERMATOPHYTOSIS

The "One Foot Treated, Other Foot Control" Technic.—Goldman and his associates [24] selected this plan in their studies of two phenylmercuric compounds. Its merit is by no means convincing. Considering the fact that the severity of ringworm on the one foot will seldom equal that on the other, and that these authors themselves observed spontaneous clearing of the control foot *pari passu* with the treated one, this method should be disregarded.

SCOPE OF SENSITIZATION IN DERMATOPHYTOSIS (EXTENDING TO BUERGER'S DISEASE?)

Although the scope of sensitization in dermatophytosis is not currently connected with war activities, it can have a bearing on members of the war forces both during and after the war. Claims for war disability may hinge on this newer development. Thompson [25] contends that the allergy of dermatophytosis may extend as far as to induce peripheral vascular disease which is of the order of, if not quite, Buerger's disease. Naide [26] has supported this thesis.

INDUSTRIAL MYCOSES IN WARTIME

Even prior to Pearl Harbor, dermatophytosis commanded attention because it was such a factor in workmen's compensation claims. After that, the additional factor of manpower in industry entered. The challenge to factory medical personnel was now shared by the United States Public Health Service. Peck, Botvinick and Schwartz [27] found that, although the fungi under laboratory conditions remained viable for at least seventy-two hours on cement, wood and copper impregnated flooring materials, the fungi could not be isolated from the flooring under field conditions. On pine wood it was viable for one week (the other flooring materials were not tested at this interval). It is not surprising to learn that native fungicidal substances are negligible in wood and cement, although more might have been expected from copper. It appears, then, that such flooring "is a possible but not likely source" for dermatophytosis and that copper impregnated flooring is not superior to others and scarcely merits the extra expense.

It is somewhat surprising that only 28 per cent of the 2,123 persons examined by Peck and his associates exhibited unequivocal clinical dermatophytosis, because statistics in other groups (students, inmates of institutions, members of the armed forces) have ranged consistently around 65 per cent. These workers were perhaps overconservative in diagnosing dermatophytosis, as they secured cultures from a goodly number of their "doubtful" cases. From calculations which we made on Peck's materials it appears reasonable to assume that upward of 50 per cent of the personnel in industry is affected by the condition.

Compulsory showers, with foot baths of hypochlorite solution, evidently did not reduce the incidence of dermatophytosis, as judged by a control group which did not receive showers. The tests lose much significance, though, because the foot baths were not rigidly administered.

It is surprising but gratifying that dermatophytosis and its allergic manifestations were not important factors in lost time among industrial workers. Most important too is the evidence of Peck and his associates in the dispute whether the allergy of dermatophytosis predisposes to the development of contact dermatitis. They concluded that it did not predispose. Industrialists should not discriminate against workers with positive Trichophytin reactions in the fear that they may be more susceptible to contact dermatitides. If 42 per cent of workers have a positive reaction, the risk would have to be accepted in any event; industry at large could scarcely visit unemployment on such a large fraction of labor. Naturally these considerations apply also to members of the armed forces in the establishments which are indispensable in the highly mechanized warfare of today, whether today or post war when disability allowances will have to be adjudicated.

24. Goldman, L.; Henningsen, A. B.; Ringelman, N. P.; Fox, H. H., and Hesselbrock, J.: Evaluation of a Fungicidal Agent for Fungous Diseases of the Feet, Arch. Dermat. & Syph. **47**: 569 (April) 1943.

25. Thompson, K. W.: Studies on the Relationship of Dermatomycosis to Ulceration and Gangrene of the Extremities, Yale J. Biol. & Med. **16**: 665 (July) 1944.

26. Naide, M.: The Causative Relationship of Dermatophytosis to Thromboangiitis Obliterans, Am. J. M. Sc. **202**: 822 (Dec.) 1941.

27. Peck, S. M.; Botvinick, I., and Schwartz, L.: Dermatophytosis in Industry, Arch. Dermat. & Syph. **50**: 170 (Sept.) 1944.

SELF TREATMENT

The treacherous ground of self treatment has been thoroughly explored by us. Although there appears to be a consensus among dermatologists against self treatment, it remains that a large section of the public will still treat itself. It buys aspirin for headache and "rheumatic pains" and will use "rhinitis" tablets and benzedrine inhalers for colds in the head. Similarly, it will attempt to avoid proper medical treatment by buying proprietary preparations for athlete's foot as long as the condition remains in the milder form that does not incapacitate. Whitfield's ointment is probably more widely known than other forms of treatment, barring the ones widely advertised by proprietary houses. It must be granted that it is harmless in the hands of many people, but a canvass of his local dermatologic society by one of us (F. D. W.) shows that there is still a large factor of danger. Thus we are defeated in our attempts to compile a list of medicaments which could be recommended safely. Only one substance, boric acid, has therapeutic value and is safe for public use. Even here there is a hazard: the public may depend on it too much; i. e., for severer forms which demand the services of the physician.

It is in this light that the program which follows has been arranged. Naturally, prophylaxis is not as highly liable to criticism as treatment, and we feel quite satisfied with the recommendations under this heading. Under the heading of treatment, though, the patient is charged with the responsibility of deciding whether his case is a mild one, and few individuals are capable of even approximating an evaluation of their diseases—even athlete's foot. This, though, seems to be the lesser of two evils, i. e. whether to recommend a substance like boric acid which can do a minimum of harm, or to condemn any and all forms of treatment. The public is bound to practice self treatment of some kind and it may be better to encourage the use of boric acid than for the public to continue the use of iodine, camphorphenol mixtures and other damaging chemicals.

In any event, if self treatment is to be attempted at all it should not exceed the principles embodied in the following abstract. It represents a digest, adapted from the body of this review, which leads to practical therapeutic applications. It must not be regarded as a self-sufficient exposition of the matter; it is subject to all of the qualifications indicated in the body of this paper.

Prophylaxis.—1. Keep the feet clean and dry, with special attention to places between the toes. Dry these carefully but not so hard as to irritate the skin.

2. Air shoes and socks when not in use.

3. Under special conditions, keep the feet elevated when at rest (where the conditions predispose to intertrigo, as with marching soldiers).

4. Shoes should be selected that are as light and well aerated as is compatible with working conditions.

5. A dusting powder consisting of 10 per cent boric acid in powdered talc should be dusted on the feet and between the toes every night and morning.

Treatment.—1. Only the mild lesions that occur between the toes should be treated by the patient himself; i. e., where the lesions exhibit only scaliness and perhaps mild redness and fissuring. Considerable redness, moisture, pustule formation or pain call for the attention of the physician and the physician only. The patient must err on the safe side.

2. Such mild cases can be treated as follows:

(*a*) Observe regulations just laid down for prophylaxis.

(*b*) Nothing is safe as a local application except the boric acid foot powder mentioned under prophylaxis. If there is not any improvement within two weeks, consult a physician.

(*c*) Under no circumstances should the patient yield to the well meant recommendations of friends and to advertisements. Preparations containing iodine, mercury or sulfur are particularly dangerous, and sulfonamide preparations are notorious because they so frequently sensitize the individual to sulfonamide drugs which may be imperatively indicated later for a really serious ailment.

CONCLUSIONS

The war has added fresh importance to dermatophytosis. This has stepped up the tempo of investigation with the natural result that certain old ideas have been confirmed, others crystallized or nearly crystallized, some disproved and others newly established. Much of this work has a foundation of the highest reliability because under war conditions it was possible to recruit expert dermatologists and mycologists, together with an adequate supply of assistants, clinical materials, laboratory facilities and funds. The results accordingly, have high and probably enduring significance.

In the way of confirming old ideas, the incidence of dermatophytosis was again found to be high. The hygiene of the feet was paramount both in prophylaxis and in treatment, with the emphasis on the detrimental role of sweat. The "old reliable" Whitfield's ointment, and also boric acid powder, stood up well as fungicide preparations when compared with newer ones like sodium propionate and Cresatin.

Changes in concepts appeared; first, the current of opinion is sweeping bacteria into the scene as the cause of many infectious intertrigos that have hitherto been taken for granted as mycotic. Other foot conditions are due to sensitization to local applications such as shoe polish and medicaments, and to long standing hypostasis and trauma. As to the notorious repetition of attacks in dermatophytosis, opinion is swinging to the belief that they represent recurrences; the extent to which they are reinfections is probably minor. This point is not merely academic; it bears on prophylaxis by indicating that efforts should be directed at the feet more than the environment, thus saving bother and expense. Foot baths (hypochlorite and hyposulfite) are becoming discredited. Evidence has been submitted in the controversy whether dermatophytosis predisposes to contact dermatitis; namely, that it does not. This question is important for adjudicating disability claims in the armed forces and elsewhere.

Fresh information is represented, first, in the establishment of a definite technic for sterilization of shoes. In treatment, sodium propionate, undecylenic acid and Cresatin (metacresylacetate) have emerged as useful fungicides. Medicine is now surprised by the theories that Buerger's disease is an allergic expression of dermatophytosis and that little manpower was lost in industry as the result of dermatophytosis. Matters are rapidly coming to a head in the establishment of a standard method for testing fungicides, at least for dermatophytosis, and an outline has been submitted for the clinical evaluation of fungicides which should be useful to manufacturers and others. Too, a venture was made into the dangerous field of self treatment.

The foregoing record of accomplishment is a credit indeed to the numerous investigators who played a part where they could in the American war effort. Their benefits to medicine will far outlast the war.

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SATURDAY, JULY 14, 1945

NEOSTIGMINE AND NEUROMUSCULAR DYSFUNCTION

Neostigmine (prostigmine), a synthetic drug, was first used in the form of the methylsulfate for stimulating the intestinal tract and thus overcoming postoperative atony. A second and even more striking clinical application was soon discovered, based on its effect on the symptoms of myasthenia gravis. Even when the drug is given by mouth as neostigmine bromide, the decrease in muscle fatigue is often striking. Moreover, neostigmine will apparently inhibit cholinesterase, the chemical agent that destroys acetylcholine, an important factor in neuromuscular transmissions. Acetylcholine is found in nerve tissue and at the myoneural junction. One theory accounts for the effectiveness of neostigmine in myasthenia gravis on the assumption that inhibition of the cholinesterase at the junction permits an impulse to pass more readily and effectively from the nerve to the muscle. Not all investigators accept this explanation, but none disagree with regard to the powerful effect of the drug when given to patients with myasthenia gravis. There is some evidence, however,, that neostigmine may affect spinal centers, as well as the myoneural junction, and possibly centers in the medulla or cerebrum. Kremer,[1] by using intrathecal injections of neostigmine, produced loss of muscle tone in man.

These studies have led to a trial of neostigmine in a wide variety of diseases in which muscular paralysis, spasm, tension or spasticity and cramps, painful or otherwise, are important symptoms. In 1944 alone studies were published also on the use of the drug in anoxia, homosexuality, pregnancy, amenorrhea, arthritis, goiter, morphine analgesia, colon dilatation and poliomyelitis.

Kabat and Knapp[2] have reported studies on patients with poliomyelitis indicating relaxation of muscular spasms, relief from pain, increasing the strength and improvement in muscular coordination after treatment with neostigmine. Trommer and Cohen[3] also noted good effect in the treatment of muscular spasm in patients with rheumatoid arthritis and some associated conditions. Kabat[4] has also indicated that this drug may have a useful function in treating hemiplegia, facial paralysis, cerebral palsy, chronic rheumatoid arthritis and subacromial bursitis. Over 50 patients with these various disorders were treated by subcutanueous injections of 1 mg. of neostigmine methylsulfate with 0.65 mg. or 0.43 mg. of atropine sulfate.

In the series treated by Kabat there were 8 patients suffering from persistent joint stiffness, pain and limitation of motion following various types of fractures. In 7 of these cases significant improvement was noted during one to two weeks of treatment. Seven patients with hemiplegia were observed with a favorable relief of their spasticity while under treatment. Similar results were reported in patients with hemiplegia due to cerebral palsy of the congenital type. Six patients with chronic rheumatoid arthritis were relieved in various degrees and, in general, Kabat felt that the results were encouraging enough to warrant further investigation with control procedures and other means of evaluation.

Schaubel[5] also has observed encouraging results with a similar form of treatment in cases of spastic cerebral paralysis.

Watkins and Brazier[6] have recently attempted to evaluate the muscle spasm in poliomyelitis by electromyographic studies. In the course of their work, seventy tests were made before and after the intramuscular injection of 1.6 mg. of neostigmine methylsulfate. At the period of maximum effectiveness of the drug, namely twenty minutes after the injection, there was less irritability exhibited in the electromyogram than during the control period. They point out that, in the treatment of poliomyelitis, neostigmine has not been used in a sufficient number of instances to justify the drawing of definite conclusions in regard to its value. Watkins and Brazier observed, moreover, the effect of only a single application and not the effect of repeated injections as used by Kabat. They conclude that the degree of change was not great enough to indicate a specific effect by neostigmine on muscle spasm. Two articles reviewing the effects of neo-

1. Kremer, Michael: Action of Intrathecally Injected Prostigmine, Acetylcholine and Eserine on the Central Nerve System in Man, Quart. J. Exper. Physiol. **31**: 337 (July) 1942.

2. Kabat, Herman, and Knapp, M. E.: The Use of Prostigmine in the Treatment of Poliomyelitis, J. A. M. A. **122**: 989 (Aug. 7) 1943.

3. Trommer, P. R., and Cohen, Abraham: The Use of Neostigmine in the Treatment of Muscular Spasm in Rheumatoid Arthritis and Associated Conditions, J. A. M. A. **124**: 1237 (April 29) 1944.

4. Kabat, Herman: Studies on Neuromuscular Dysfunction: I. Neostigmine Therapy of Neuromuscular Dysfunction Resulting from Trauma: II. Neostigmine Therapy of Hemiplegia, Facial Paralysis and Cerebral Palsy; III. Neostigmine Therapy of Chronic Rheumatoid Arthritis and Subacromial Bursitis, Pub. Health Rep. **59**: 1635 (Dec. 22) 1944.

5. Schaubel, H. J.: Prostigmine as an Adjunct in the Treatment of Spastic Cerebral Palsy, Physiotherapy Rev. **24**: 236 (Nov.-Dec.) 1944.

6. Watkins, A. L., and Brazier, M. A. B.: Observations on Muscle Spasm in Poliomyelitis: Electromyographic Studies on the Effect of Various Forms of Thermal Therapy and of Prostigmine, Arch. Phys. Med. **26**: 325 (June) 1945.

stigmine on patients with poliomyelitis appeared in THE JOURNAL last week.[7]

Although neostigmine may be of value in treating conditions other than intestinal atony and myasthenia gravis, the work presented by Kabat and others on its use in a large number of unrelated conditions is insufficient for critical evaluation. More carefully controlled studies will be required before a definitive statement with regard to its usefulness can be made.

HEALTH AND PHYSICAL EDUCATION LEGISLATION IN OREGON

The Forty-Third Legislative Assembly of the State of Oregon passed House Bill No. 53, entitled "An act to provide for programs of health instruction and physical education in all elementary and high schools of the state, to provide for the planning, supervision, direction and evaluation of such programs by the superintendent of public instruction, and appropriating money therefor . . ." and to repeal certain other sections of existing statutes. The bill, if one may judge from a story by Wilma Morrison in the Portland *Oregonian*, April 8, attracted little attention in the legislature and calls for only $26,000 a year from the taxpayers. The law provides that all school districts in the state of Oregon shall—not may—provide in their respective schools programs of health instruction and physical education for the development of health and physical fitness for all elementary and high school pupils in such schools. The purpose is to promote, develop and maintain among pupils at all levels "optimum physical growth, health and physical fitness." The bill prescribes what shall be included in health instruction programs, namely "personal hygiene, community health and sanitation, communicable diseases, nutrition, mental health, safety education, first aid, instruction in the choice and use of health services and health practices, instruction concerning the structure and functioning of the human body, the physiological effects of exercise, and such other instruction as the state superintendent of public instruction may deem important."

The program in Oregon is to be under the general direction of the superintendent of public instruction. Six mandatory functions are assigned to him: to (1) provide health examinations in the elementary and secondary schools, (2) provide and recommend program materials, (3) provide checks and standards by which the progress of individual pupils and the programs of schools can be evaluated and the schools rated "in terms of their meeting the purposes of this act," (4) coordinate the activities of governmental agencies which carry on functions in the schools related to the purposes of the act, (5) employ the necessary personnel and (6) make necessary rules and regulations.

Subordinate school officials in local governmental units are made responsible for carrying out the rules and regulations issued by the superintendent of public instruction. Exemptions are provided for constitutional or religious objectors who may wish to be excused from participation in the program outlined by the act.

Responsible officials in Oregon met at once in order to put the provisions of the act into effect. The superintendent of schools has created an Oregon Joint Committee on Health and Physical Fitness, headed by Dr. R. W. Leighton, dean of physical education at the University of Oregon. This is the group which formulated the bill. A prime force in getting the legislation passed was the Oregon State Federation of Women's Clubs. The appropriation is small, although Dean Leighton says it will be sufficient. With existing buildings and equipment, supervision from trained personnel and the setting up of standards, results should follow.

The Oregon act is said to be the first legislation of its type in any state. Legislation, or even the effective functioning of the program under such legislation as this, will not necessarily eliminate all physical unfitness and all sources of poor health. Much can undoubtedly be accomplished, but not in a year or in two years. Measurable results may take ten years. In the meantime, those who work in the program and those who appropriate money for its support must not become discouraged. Even with the best program functioning at the highest possible efficiency some conditions are not remediable in the present state of medical knowledge. The time is ripe for great progress toward improved health and physical fitness.

Current Comment

TRANSMISSION OF A SHOCK PRODUCING FACTOR

Shock is still one of the important causes of death of the injured soldier. While the symptoms and various physiologic responses of the shock syndrome are well known, the causative factors are still in doubt. One of the difficulties facing experiment in this field is the production of a reproducible shock syndrome. This has been accomplished to some extent by either traumatizing the leg of an experimental animal or by leaving a tourniquet on the leg for a time and then removing it. By using such a standardized technic Cannon and Bayliss concluded that there is a toxic substance emitted from the injured tissue which is responsible for the production of the general shock syndrome. Additional work has been attempted to show that a toxic agent is responsible for the initiation

7. Brainerd, Henry; Katz, H. J.; Rowe, A. P., Jr., and Geiger, J. C.: The Clinical Manifestations of Poliomyelitis, J. A. M. A. **128**: 718 (July 7) 1945. Fox, M. J., and Spankus, W. H.: The Value of Neostigmine in Acute Anterior Poliomyelitis, ibid. **128**: 720 (July 7) 1945.

of shock. Recently Rapport, Guild and Canzanelli [1] produced shock by allowing a tourniquet to remain on the leg of a rabbit for two hours. To show the presence of a toxic substance the rabbit's leg was joined into the general circulation of a second, normal, rabbit. Thus the traumatized leg received all of its blood supply from the normal rabbit's circulation and in turn contributed its blood and tissue metabolites to the normal rabbit's circulation. This experimental procedure, called "cross circulation," is a common though difficult physiologic testing device. In the control experiments in which normal legs were cross circulated with a normal rabbit the animals survived for fifteen and a half hours. When the tourniquet treated legs were cross circulated with normal rabbits the animals survived only four and three-tenths hours. These observations seem to point to the possibility that a shock producing factor was transmitted in the blood. The knowledge that a toxic substance may be liberated from an injury which is of such extent that the host is thrown into shock may have considerable directive influence both in the prevention and in the treatment of the shock syndrome.

PROGNOSIS IN THROMBOCYTOPENIA

In a study of 30 cases of thrombocytopenic purpura Schwartz [1] showed that increased numbers of eosinophils in the bone marrow signify a favorable prognosis for spontaneous recovery, while scant numbers suggest a chronic course and the necessity for splenectomy. The marrow eosinophilia probably indicates an allergic state, while thrombocytopenia represents a sensitization reaction involving the megakaryocytes. Neutrophils were selected as cells for the basis of comparison, because eosinophils presumably arise from the same stem and because specific stimulation of the granulocytes does not occur in thrombocytopenic purpura. The number of eosinophils observed in counting 1,000 granulocytes of the neutrophilic series was determined on the basis of these studies. Schwartz feels that it is possible to divide cases of primary thrombocytopenic purpura, at least from the prognostic point of view, into two types: (*a*) those with increased numbers of eosinophils in the marrow and (*b*) those without increase in marrow eosinophils. Cases with high marrow eosinophils are probably due to sensitivity, are usually acute in onset and course, occasionally follow infection or ingestion of drugs or allergenic foods, have relatively benign course and are followed by complete clinical and hematologic recovery. Splenectomy is not necessary in these cases, and blood transfusions hasten recovery. Prognosis in cases with few eosinophils, arbitrarily below 50, are of poor prognostic outlook and require splenectomy. Correlation was not found between the marrow eosinophilia and peripheral blood eosinophilia. Schwartz is aware that prognoses based on the numerical variation of a certain cell must be made with caution and that a number of factors can influence the bone marrow at a given moment. It is suggested, however, that certain correlations do exist and that these may be utilized in helping to make prognosis and treatment of thrombocytopenic purpura more rational.

1. Rapport, D.; Guild, R., and Canzanelli, A.: Am. J. Physiol. **143**: 440 (March) 1945.

1. Schwartz, S. O.: The Prognostic Value of Marrow Eosinophils in Thrombocytopenic Purpura, Am. J. M. Sc. **209**: 579 (May) 1945.

THE 1942-1943 EPIDEMIC OF INFANTILE PARALYSIS IN MALTA

In the middle of November 1942 an epidemic of infantile paralysis began in Malta, reached its height in the latter part of December and was over by March 1, 1943. The outbreak included 483 paralytic cases, 426 in civilians and 57 in military service men. Owing mainly to circumstances connected with the bombardment of Malta, satisfactory study could not be made of the occurrence of civilian nonparalytic cases. Of the 483 cases, which include 40 simultaneous cases on the neighboring island of Gozo, 397 (82 per cent) occurred in children under 5 years of age. The case death rate in the civilians was 6.1 and in the service men (United Kingdom) 19.3 per cent. These and other facts to be cited are taken from the report of epidemiologic features of the outbreak by Seddon and his co-workers.[1] Like studies of other epidemics in isolated regions, their study presents results of interest in regard to the origin and spread of outbreaks of infantile paralysis. After thorough consideration of the circumstances, some of which are quite unusual, it seemed safe to conclude that the spread of the Malta epidemic was not promoted by the great overcrowding at that time, by the lack of food and vitamins, by possible contamination of food and water from the use of sewage for manuring or by the consumption of dried milk. As the epidemic developed rapidly at a time when flies were less numerous than at other seasons, "it is tolerably certain that the disease was not spread by flies." That the virus of the epidemic was an indigenous strain is indicated by the facts that a few sporadic cases of infantile paralysis have developed in Malta over many years, that civilians were attacked first, that the adult Maltese almost wholly escaped and that there was no evidence of the virus being brought in by service men. Seddon and his associates point out that the causal strain "cannot have differed greatly from the normal strain, since its pathogenicity was confined to the more susceptible groups of the indigenous population, who had presumably not had time or opportunity to become completely protected by the normal process of latent infection." They also note that the pattern of the epidemic corresponds to that of a respiratory type of infection. But why did the disease assume the paralytic form? "The virus is constantly with us, constantly infecting us, but only rarely getting through to attack the central nervous system. And the circumstances in which it loses its temper, so to speak, and gores us to the marrow we simply do not know." [2]

1. Seddon, H. J.; Agius, T.; Bernstein, H. G. G., and Tunbridge, R. E.: The Poliomyelitis Epidemic in Malta, 1942-1943, Quart. J. Med. **14**: 1 (Jan.) 1945.

2. Poliomyelitis in Malta, Annotation, Lancet **1**: 667 (May 26) 1945.

MEDICINE AND THE WAR

ARMY

ARMY MEDICAL OFFICERS REQUEST ROTATION OF ASSIGNMENTS IN SERVICE

NOTE.—The following communication received from five medical officers of the United States Army in Europe, including a major and four captains, is published so that it may receive consideration by the medical profession and by the officers in the Office of the Surgeon General. Contrary to our usual custom, the letter is printed without signature, since the officers specifically request that their signatures be not included. Certainly the point raised merits consideration.—ED.

To the Editor:—We are army medical officers on active duty for varying lengths of time ranging from thirty-two months to forty-eight months at a fighter station in England since November 1943 and are now about to go to Germany in the Army of Occupation. When we shall be relieved is a matter of speculation. Frankly, we've been thinking lately about the lack of rotation for medical officers and naturally the question arises "Are there not sufficient doctors in the United States to meet our country's military demands?" We think there are.

There are many conflicting reports reaching us concerning the procurement of medical officers for military service, none of which, however, are of an official nature. In order to ease our minds, and to be sure they need easing, we medical officers would like some clarification of the subject if possible. We would like the following information answered:

(*a*) The number of medical officers on active army service and naval service (excluding Veterans Administration).

(*b*) The number of medical school graduates since 1941 and the percentage of these in army service and naval service.

(*c*) The number of doctors under 45 years of age in civilian practice.

(*d*) The number of doctors being procured monthly for army service and naval service.

(*e*) The actual strength of the Army and Navy Medical Corps and the proposed strength necessary to defeat Japan.

(*f*) The number of medical officers in the Army and Navy being discharged monthly exclusive of those discharged for incapacitating medical defects.

We medical officers, like thousands of other doctors, entered the service voluntarily with the sincere belief that it was our duty and with the further belief that it was our war. We further believe that it is the war of everybody in the United States and that equal responsibility exists for every one to share in the conflict. In other words, from the view of the doctor in service, it is as much Dr. Jones's war as it is Dr. Smith's war. We are all familiar with the apparent ease with which many individuals escape military service and are of the opinion that the fault more often than not lies in our administrating agencies. We feel that inefficient medical administration has gone far enough and that if it is permitted to continue unchecked it will affect not only the medical future of the physician but also that of the layman.

We doctors in the service consider it our duty and privilege to attend the sick and wounded and would continue to feel that way if we knew we were not being forgotten. Reports are now reaching us that many doctors coming out of internships are permitted to go on their merry way into residencies, hospital appointments and practice and that there are many men of our age and training still in our home towns, unmolested by our procurement agency. If this is correct and it appears so, what about us already in service. Are we to carry the whole burden? Or isn't it their war too?

It appears now that officers are to be discharged on the point system, that is all officers except medical officers—why? Are medical officers now in service to be penalized for taking the trouble and sacrifices to earn a medical education? We cannot help but believe that the procurement of medical officers should go on strenuously as long as war exists and as long as doctors are needed in the service, so that a definite surplus should exist. In this way a discharge system could apply to the medical profession also, and no one doctor need worry that no relief is coming. In most cases rotation would go on in a most natural manner. The civilian supply of doctors would not be affected, for outgoing medical officers would take the place in civilian practice of newly "procured" doctors. Further, no one proportion of doctors would suffer degeneration of their medical knowledge and ability, as is the case now with tactical unit doctors whose main duty is holding sick call, treating colds, corns, epidermophytosis and small lacerations. Any worthwhile cases by reason of the army medical setup must be transferred to station or general hospitals many miles away for definitive treatment. As a result we see these patients only when they are transferred and then discharged to duty. As is readily seen, any professional ability we possessed on entrance into the Army is steadily deteriorating.

It is discouraging for us to see a War Department statement in the public press that the army quota for medical officers is filled and that it is contemplated that the procurement of doctors is to relax. The quota should never be filled as long as war goes on. Any quota should include plans for release of medical officers long in the service. It is conceivable that every doctor in the United States, with certain exceptions for age, disability and the like, would see military service if the war should last long enough, which is as it should be if our premise that it is everybody's country and everybody's war is correct. At this point it appears obviously to be correct. Should Dr. Smith go to war for his home and family? The answer is yes! Furthermore, should he go to war also for Dr. Jones's home and family? The answer is no! Let Dr. Jones go to war for his own family and home. For certain reasons they may not be able to go together or at the same time, but let them go consecutively. Are the newly graduated doctors to be permitted to engage in prolonged internships and even longer residencies, not to mention civilian practice, simply because it is expedient for the Army to solve the medical problem in this manner, or are these young doctors to be inducted into the service so that we who have already served three or more years may be released to take care of the country's civilian needs, not to mention the furtherance of our own medical education, which in most cases has been interrupted by our army service.

There are many physicians of our own ages who have been declared so-called "essential" doctors simply because of circumstances placing them in such a position. Let us not forget that the fallacy of this premise lies in the fact not that the individual doctor is "essential" but that the position is essential. We feel that it is high time many of these men were inducted and replaced by medical officers with years of service, who will be only too eager to become "essential" in their stead.

We are submitting the foregoing plea for your consideration in the hope that our voices added to those of many other medical officers, who even though they have not made public their sentiments are of the same opinion, will bring about a change in the policy of the U. S. Army toward medical officers. We realize that this policy cannot be affected directly by you, but there is no question in our minds that the most potent organ for public feeling in medical circles is the American Medical Association and that if the minds of American medical men are expressed by the Association the effect of its influence must certainly bring about changes in higher places.

Our only desire is "Let us be heard!"

SURGICAL CONFERENCE OF THE SIXTH SERVICE COMMAND

A two day surgical conference, sponsored by the Sixth Service Command and open to the medical profession, will be held at the John B. Murphy Memorial Auditorium, American College of Surgeons, 50 East Erie Street, Chicago, July 27-28. The conference will be opened by Col. Don G. Hilldrup, surgeon, Sixth Service Command, and the following papers will be presented:

Symposiums on Reconstructive Operations for Large Defects in Bone, Major Joseph Farrington and Major Carl G. Caspers, Mayo General Hospital, Galesburg, Ill.; Lieut. Col. Thomas Horwitz and Lieut. Richard Lambert, Vaughan General Hospital, Hines, Ill.

Osteomyelitis of the Os Calcis, Lieut. Col. Francis M. McKeever and Capt. Ronald M. Buck, Percy Jones Hospital Center, Battle Creek, Mich.

Late Closure of War Wounds Associated with Chronic Osteomyelitis, Lieut. Col. Thomas Horwitz and Lieut. Richard Lambert, Vaughan General Hospital.

Preliminary Report on the Use of Sheet Nylon in Surgery, Lieut. Col. Philip Lewin and Capt. I. Joshua Speigel, Mayo General Hospital.

Treatment of Decubitus Ulcer in the Paralyzed Patient, Lieut. Col. John H. Gibbon Jr. and Lieut. Leslie W. Freeman, Mayo General Hospital.

Derangement of the Patellofemoral Joint (Motion Pictures), Major Francis E. West, Gardiner General Hospital, Chicago, and Lieut. Col. Ralph Soto-Hall, Headquarters Sixth Service Command, Chicago.

Visceral Injuries Associated with Compound Fractures of the Pelvis, Major George B. Sanders, Vaughan General Hospital.

Surgical Technic of Amputations, Capt. Curtis M. Hanson, Percy Jones Hospital Center.

Plastic Repair of Injuries of the Penile Urethra, Lieut. Col. Justin J. Cordonnier, Gardiner General Hospital.

Experience in the Treatment of 170 Traumatic Aneurysms, Major Harris B. Shumacker, Mayo General Hospital, followed by a discussion by Col. Daniel C. Elkin, Ashford General Hospital, White Sulphur Springs, W. Va., and Comdr. Emile Holman, U.S.N.R., Naval Hospital, Shoemaker, Calif.

Primary Malignant Tumors of Bone, Lieut. Col. Joseph C. Bell, Major Gilbert W. Heublein and Major Sylvan E. Moolten, Percy Jones Hospital Center.

Continuous Spinal Anesthesia (Motion Pictures), Major Edward B. Tuohy, Percy Jones Hospital Center.

Peripheral Nerve Lesions:

(*a*) New Methods of Electrodiagnosis, Lieut. Yvo T. Oester, Percy Jones Hospital Center.

(*b*) Surgery of the Posterior Interosseous Nerve, Lieut. Col. Frank E. Mayfield and Lieut John H. Mayer Jr., Percy Jones Hospital Center.

(*c*) Surgical Treatment of Injuries of the Brachial Plexus, Capt. I. Joshua Speigel and Lieut. Richard H. Upjohn, Mayo General Hospital.

(*d*) One Stage Operations for Combined Bone and Nerve Defects, Major Joseph Farrington and Capt. I. Joshua Speigel, Mayo General Hospital.

Heavy Resistance Exercises (Motion Pictures), Capt. Thomas L. DeLorme, Gardiner General Hospital.

Surgery of the Sympathetic System:

(*a*) Causalgia, Lieut. Col. Frank E. Mayfield and Lieut. Jack C. Ulmer, Percy Jones Hospital Center.

(*b*) Vascular Disorders, Major Harris B. Shumacker, Capt. Paul B. Olsson and Capt. Kenneth L. Carter, Mayo General Hospital.

In connection with the conference, the following scientific exhibits have been proposed:

Urolithiasis in Patients with Femoral Fractures, Lieut. Col. Louis D. Smith and Capt. Stuart W. Russell, Mayo General Hospital.

Glass Cloth for Wound Dressings, Capt. Ronald M. Buck, Percy Jones Hospital Center.

Orthopedic Splints, Lieut. Col. Philip Lewin, Mayo General Hospital.

Continuous Local Penicillin Therapy in Maxillary Sinusitis, Major Richard P. Good, Vaughan General Hospital.

Femoral Fractures, Lieut. Col. Ralph Soto Hall, Headquarters Sixth Service Command, and Lieut. Col. Thomas Horwitz, Vaughan General Hospital.

Artificial Eyes, Capt. R. M. Grassle, Gardiner General Hospital Occupational Therapy, Vaughan General Hospital.

Surgical Repair of Skull Defects with Tantalum Plate (a review of existing technics), Capt. I. Joshua Speigel and Lieut. Howard R. Hamlin, Mayo General Hospital.

Dermometry, Lieut. Howard R. Hamlin, Mayo General Hospital.

Tendon Transplants, Lieut. Col. Philip Lewin and Capt. Albert O. Singleton, Mayo General Hospital; Capt. Charles Schroeder, Camp Grant Station Hospital, Ill.

MISCELLANEOUS

KELLOGG FOUNDATION EDUCATION PROGRAM FOR VETERANS

The president of the W. K. Kellogg Foundation, Dr. Emory W. Morris, has announced a program under which funds will be available to assist a limited number of medical schools in the United States and Canada in developing comprehensive programs of graduate and postgraduate medical education. The immediate objective of the program is to help extend educational facilities for medical veterans. The long range objective is to encourage schools to develop permanent programs of postgraduate medical education.

The foundation has long been interested in medical education, especially at the postgraduate level. It believes that medical schools should accept the responsibility of providing not only good undergraduate and graduate medical education but also continuing or postgraduate education for all the physicians practicing in the area which the school serves.

Under this program requests for funds have already been approved for the University of Illinois College of Medicine, the University of Minnesota Medical School, the University of Oregon Medical School, Columbia University College of Physicians and Surgeons, Cornell University Medical College and New York University College of Medicine.

WARTIME GRADUATE MEDICAL MEETINGS

The following subjects and speakers for Wartime Graduate Medical Meetings have just been announced:

California

A. A. F. Regional and Convalescent Hospital, Santa Ana Army Air Base: The Cancer Problem in the Service, Lieut. J. S. Binkley, July 17.

A. A. F. Regional Hospital, March Field: Communicable Diseases, Major Norman Nixon and Capt. Charles D. Marple, July 17.

U. S. Naval Hospital, Long Beach: Penicillin and Its Use in Syphilis and Gonococcic Infections, Lieut. Comdr. W. W. Luemling, July 18.

U. S. Naval Air Training Station, San Diego: Classification and Diagnosis of the Anemias, Dr. Alvin Foord, July 20.

Station Hospital, Camp Cooke, Lompoc: Plastic Surgery in Defects of the Head and Neck, Dr. Edward S. Lamont, July 18.

Hoff General Hospital, Santa Barbara: Plastic Surgery in Defects of the Head and Neck, Dr. Edward S. Lamont, July 18.

Indiana

Billings General Hospital, Fort Benjamin Harrison: Peptic Ulcer, Gallbladder and Liver Diseases, Drs. W. D. Gatch and Lowell D. Snorf, July 18.

Wakeman General Hospital, Camp Atterbury: Chest Diseases and Diseases of the Larynx, Dr. Henry C. Sweany, July 18.

Wisconsin

Station Hospital, Camp McCoy: Plexus and Peripheral Nerve Injuries, Dr. Theodore C. Erickson, July 18.

Station Hospital, Truax Field: Endocrinology, Dr. W. D. Thompson, July 18.

Illinois

Gardiner General Hospital, Chicago: Bone and Joint Infections, Dr. David E. Markson and Major Sam W. Banks, July 18.

Station Hospital, Fort Sheridan: Repair of Bone in Fractures and Diseases, Drs. James R. Regan and Edwin Ryerson, July 18.

Vaughan General Hospital, Hines: Laboratory Diagnosis and Its Relationship to Medical and Surgical Treatment, Dr. Edwin F. Hirsch, July 18.

Mayo General Hospital, Galesburg: Blood Dyscrasias—Malaria—Filariasis, Dr. Raphael Isaacs and Col. Alexander Marble, July 18.

Regional Hospital, Chanute Field, Rantoul: Mental Hygiene and the Prevention of Neuroses in War, Col. William J. Blackwenn, July 18.

ORGANIZATION SECTION

Washington Letter

(From a Special Correspondent)

July 9, 1945.

Fulbright Advocates Formation of Bureau of Scientific Research

Senator Fulbright has introduced a bill to establish a Bureau of Scientific Research in the Department of Commerce, which he says is designed to afford a medium through which new inventions may be properly developed with federal aid and made available to small industry or individuals who may desire to enter business. He believes it will be helpful to returning war veterans. "There is a real need for the utilization of existing patents in the interest of the people," he said, "and to encourage the latent inventive possibilities of the nation, through the elimination of existing handicaps and encouragement of small industries to seek and use such ideas." He explained that the bureau would be authorized to procure the services of leading scientists, engineers, chemists and other professional experts, to provide small enterprises with the best possible research facilities. The bill proposes to promote in the national interest the fullest and speediest introduction of new technics in science and invention and in manufacturing, communication and other phases of productive activity; also to promote the maintenance of free enterprise by making available to small and medium size business concerns scientific and technical inventions, products and processes and to establish a central scientific and technical office to assure the maximum use of these.

Facilities for Psychoneurotic Veterans Termed Inadequate

Newspaper reviews of the facilities for psychoneurotic war veterans charge that the medical profession is not prepared to care for these patients. "A staggering need for the creation of psychiatric facilities for the care of the mentally disabled" is reported by the National Committee for Mental Hygiene, which reports that twenty-five states do not have one community clinic for psychiatric care and that there are "vast areas" without doctors trained for this work. In the United States only 139 hospitals and clinics are ready to treat mental casualties. Only 30 neuropsychiatric hospitals are operated by the Veterans Administration, which has resulted in overcrowding and lack of outpatient care, according to the committee. While the war has increased the number of mental patients—half a million veterans have been discharged for psychiatric reasons and another half million are expected before war's end—the number of doctors to treat them has been reduced. A congressional inquiry revealed that care of psychoneurotic veterans is inadequate in veterans' hospitals, although the number of patients is growing. The situation is said to pose a big problem for Gen. Omar Bradley when he takes over the Veterans Administration.

Tuberculosis Experts Testify at Kelley Hearing

Army, Navy, Selective Service and civilian tuberculosis experts were to testify today and tomorrow before the committee headed by Representative Augustine B. Kelley of Pennsylvania to study aid to the physically handicapped. Hearings were to be resumed in room 429 of the Old House Office Building. Those who testified today were Col. Esmond R. Long, chief consultant on tuberculosis, Office of the Surgeon General, U. S. Army; Dr. Louis E. Siltzbach, Committee for the Care of Jewish Tuberculous; Capt. Robert Duncan, commanding officer of the Bureau of Medicine and Surgery at Bethesda, Md., U. S. Navy; Mr. Holland Hudson, National Tuberculosis Association and National Rehabilitation Council; Lieutenant Colonel Coatsworth, Selective Service System; Dr. Herman E. Hilleboe, U. S. Public Health Service Tuberculosis Control Division; Mr. Edward Hockhauser, Committee on Care of Jewish Tuberculous, and Mr. Edward K. Funkhouser, District of Columbia Tuberculosis Association.

Liberated War Prisoners Recovering Quickly

American prisoners of war released from German prison camps are recovering quickly and completely from malnutrition caused by starvation, according to a study based on 275 severe cases at the 217th General Hospital in Paris, released by the Office of the Surgeon General, U. S. Army. Lieut. Col. Don C. Wakeman, chief of medical service of the hospital, said that "a survey was made to determine the average daily gain of weight in uncomplicated cases of malnutrition, and those who had lost more than 25 pounds gained an average of 1⅕ pounds a day during an average observation period of twenty-five days." In milder cases six feedings a day are given of a high caloric and high vitamin diet, with supplementary vitamin preparations for those showing specific vitamin deficiency states. In the more severe cases there was inability to tolerate a sufficient quantity of food to allow recovery through feeding alone, and intravenous solutions, common blood plasma and transfusions of whole blood were necessary to get patients into condition where food would be tolerated. X-rays of patients with nausea, vomiting, diarrhea and intolerance to food showed changes in functions of the intestine resembling those of sprue. Considerable improvement was noticeable in two weeks.

Judge Vinson's Point of View Regarding Taxation

The medical profession may not be in complete harmony with the views on taxation of Judge Fred M. Vinson, chosen by President Truman to be secretary of the treasury in succession to Henry Morgenthau. While he believes that excess profits taxes on business should be repealed immediately after Japan is whipped, and he would write postwar tax bills to encourage capital taking job-making risks, he also believes that the personal income tax base should be broad, with lower exemptions than at present. Mr. Vinson is the fourth man with congressional experience to be brought into the Truman cabinet. The others are Secretary of State James F. Byrnes, Secretary of Agriculture Anderson and Secretary of Labor Schwellenbach.

Red Cross Launches Drive for Hospital Workers

The American Red Cross seeks 750 qualified social workers and 600 recreation workers for immediate duty in military hospitals rapidly filling with sick and wounded servicemen from the Pacific and European theaters. With demobilization in Europe, the wounded are returning so fast that the Red Cross has had to expand its hospital program.

Medical Legislation

MEDICAL BILLS IN CONGRESS

Drugs

At the request of the administrator of the Federal Security Agency, S. 1217 was introduced July 2 by Senator George, Georgia, to provide for the free importation of substances, together with their containers and other articles in use at the time of importation for the protection or preservation thereof, entered or withdrawn from warehouse by or for the account of the board of trustees of the United States Pharmacopeial Convention, or the Council of the American Pharmaceutical Association, for use by or on behalf of that board or that council in connection with the establishment by that board or the Committee on National Formulary of standards for the manufacture or control of medicinal products.

Veterans Administration

Representative Rogers, Massachusetts, has introduced H. R. 3685, proposing that any veteran who as a result of service connected disability is so helpless as to be in need of a nurse or attendant shall be granted an allowance of $100 a month in addition to any pension or compensation to which he is otherwise entitled under laws administered by the Veterans Administration.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

CALIFORNIA

Prisoners Volunteer for Experiment with Bubonic Plague.—More than 100 San Quentin prisoners recently volunteered for the government's investigation of bubonic plague. Fifty selected men were inoculated with the new vaccine of the George Williams Hooper Foundation of the University of California under a research program sponsored by the Office of Scientific Research and Development, according to the San Francisco *Chronicle*.

Eric Liljencrantz Memorial.—The Hewlett Club of Stanford University School of Medicine has established the "Eric Liljencrantz Memorial Collection on Aviation Medicine" in the Lane Medical Library. Dr. Liljencrantz graduated at Stanford medical school in 1929 and was assistant professor of medicine (radiology) at the time he entered service. A bronze tablet commemorating the service and untimely death of Commander Liljencrantz has been set up at the Naval School of Aviation Medicine, U. S. Naval Air Station, Pensacola, Fla., where he lost his life in an airplane crash Nov. 5, 1942, while studying the physiologic effects of acceleration.

Diabetic Children's Camp Opens.—Camp Whitaker, said to be the only camp for diabetic children on the West Coast, will open for the eighth consecutive year from July 22 to August 19. The camp is under the direction of Dr. Mary B. Olney, assistant professor of pediatrics, University of California Medical School, San Francisco. It is located in the Sierras at an altitude of 5,600 feet, is 60 miles east of Fresno and adjoins the General Grant Grove section of Kings Canyon National Park. The camping period is divided into two periods of two weeks each at a cost of $35 each period plus transportation. There are several camp scholarships available. Applications should be made to Dr. Olney at the University of California, San Francisco.

GEORGIA

University News.—Dr. Edward J. McCormick, Toledo, Ohio, chairman of the Council on Medical Service and Public Relations, American Medical Association, gave the commencement address at the University of Georgia School of Medicine, Augusta, June 11, on the present trend in medical care.

Personal.—Dr. John H. Walker, Atlanta, has been appointed pediatric consultant to the division of maternal and child health of the Georgia Department of Public Health, succeeding Dr. Paul R. Ensign, who is now director of the maternal and child health division of the Kansas State Board of Health, Topeka (THE JOURNAL, April 21, p. 1066).——Dr. Rufus F. Payne, Atlanta, assistant health officer in Fulton County, has been appointed medical superintendent of the State Tuberculosis Sanatorium at Alto.——Dr. John M. Walton, Atlanta, has been named associate medical director of the Southeastern area of the American Red Cross.

ILLINOIS

Personal.—Dr. Willis I. Lewis, Herrin, was elected president of the Williamson County Health Council at its meeting May 14.——Dr. and Mrs. Emerson M. Brewer, Rantoul, observed their fiftieth wedding anniversary recently.

Chicago

Symposium on Forensic Medicine.—The committee on local medicolegal problems of the Institute of Medicine of Chicago, with assisting societies of physicians and lawyers, will hold a symposium on six Monday evenings beginning September 24 through October 29, the subjects selected being especially planned for pathologists, physicians, lawyers, toxicologists and others interested in forensic medicine. Each subject will be introduced with a formal discussion by a physician and a lawyer, followed by a panel discussion and question period. A complete program will be available later.

Industrial Health Committee.—The Chicago Industrial Health Committee is the name tentatively selected for an organization now being developed for Chicago and Cook County. The project is being formed to provide industrial workers in participating industries with continuous and authentic health information on vital health problems and to promote the utilization of procedures, such as Kahn tests, chest x-rays and vision testing, to be made available through cooperating health agencies as requested and available. The entire project will be set up as a health education program. The movement has been endorsed by the American Association of Industrial Physicians and Surgeons, the Council of Social Agencies of Chicago, the Chicago Medical Society and Chicago Health Department, the educational committee of the Illinois State Medical Society, the City of Chicago Municipal Tuberculosis Sanitarium, Chicago Dental Society, Chicago Society of Industrial Physicians and Surgeons, industrial hygiene division of the state department of public health, industrial nurses section of the Illinois State Nurses Association, the Cook County Public Health Unit and others. Efforts are now being made to obtain a full time executive secretary. Additional information may be obtained from Dr. Frederick W. Slobe, 2024 South Western Avenue.

Country Home for Convalescent Children Sold.—The University of Chicago has sold the property of the Country Home for Convalescent Children at Prince Crossing, near Wheaton, to Wheaton College, according to an announcement June 29. The Wheaton College Academy will be transferred in September to the new site and buildings, which will provide accommodations for 125 boarding and 75 commuting students. The sale reflects the fundamental changes in methods of treating crippled children since the Country Home was founded in 1914. While formerly the general method of treatment was largely by immobilization in casts, today bone and joint deformities and diseases are generally corrected or cured by surgery, with such relatively brief periods of convalescence that the number of patients in the Country Home has dwindled steadily. In a statement, Frederic C. Woodward, LL.D., chairman of the board of trustees of the Country Home, said that the changes in methods of handling orthopedic cases have so greatly reduced the time of convalescence that the home at no time in the past five years has operated at more than half of its bed capacity. In the last year occupancy has never risen above 20 per cent, making maintenance costly beyond all proportion to the benefits derived. There has also been a trend away from placing children in institutions, away from their family environment, he said; it is now considered better practice to keep the children at home as much as possible and provide medical care with a minimum of separation from the family. Transfer of the work to the campus will avoid further waste of charitable funds and ineffective use of medical personnel. The 18 patients now at the home will be transferred either to the University of Chicago clinics or to medical agencies from which they were referred to the home. The Country Home, founded by the late William J. Chalmers, of the Allis-Chalmers manufacturing firm, and his wife, became affiliated with the university in 1927 and was amalgamated in 1938. The several memorial funds which have sustained the home will be continued, with preservation of memorial tablets, under present plans, which call for the erection of a new building near the university within two years. This building will be established as a permanent memorial to Mr. and Mrs. Chalmers and will form part of the integrated medical center at the university, Mr. Woodward stated.

MASSACHUSETTS

License Changes.—The board of registration in medicine on June 6 took the following actions:

Dr. Julius Shubert, Boston, license revoked for not less than three years because of gross misconduct in the practice of his profession, as shown by collusion.

Dr. Pasquale E. Massa, Boston, license suspended for a period of one year because of gross misconduct in the practice of his profession, as shown by violation of the narcotic law and conspiracy to violate this law (THE JOURNAL, June 30, p. 679).

Dr. Ralph K. Coleman, Arlington, license restored to practice medicine in Massachusetts.

Medical Schools Combine in Commencement Exercises.—In the first ceremony of its kind, 292 recent medical and dental graduates of Harvard University, Tufts College and Boston University received army and navy commissions June 23 in combined exercises in the Harvard Medical School Quadrangle. The army commissions were awarded by Major General Sherman Miles, commanding the First Service Command, the Navy by Rear Admiral Felix Gyax, commandant of the First Naval District. Major General Norman T. Kirk, Surgeon General of the Army, gave the principal address. Other speakers were Leonard Carmichael, LL.D., president of Tufts, and James B. Conant, LL.D., president of Harvard. Daniel A. Marsh, LL.D., president of Boston, observed that the first combined exercises of the three schools of medicine demonstrated the spirit of cooperation in medical education.

MICHIGAN

Hardy Kemp Named Dean.—Lieut. Col. Hardy A. Kemp, M. C., secretary of the Army Medical School, Washington, D. C., has been appointed dean of the Wayne University College of Medicine, Detroit. Colonel Kemp graduated at St. Louis University School of Medicine in 1926 and prior to his entrance into the service was dean of the Ohio State University College of Medicine, Columbus, Ohio.

MISSISSIPPI

Personal.—Dr. Thomas K. Chandler Jr., Tunica, director of the Tunica County Health Department, has been appointed to a similar position in Coahoma County, succeeding Dr. Guy R. Post, who has become medical director of the crippled children's service and medical consultant of vocational rehabilitation for the state (THE JOURNAL, March 10, p. 606).——Dr. James P. Sharon, who has been acting director of the Marion County Health Department, Columbia, has resigned, effective May 15.

NEW JERSEY

Joseph Buch Dies.—Joseph G. Buch, director of the New Jersey Rehabilitation Commission and chairman of the state crippled children's commission, died at his home in Trenton, June 21, of coronary thrombosis, aged 63.

Special Society Election.—Dr. Harry J. Perlberg, Jersey City, was chosen president of the Radiological Society of New Jersey at its annual meeting May 16. Other officers include Drs. John L. Olpp, Englewood, vice president; Harry R. Brindle, Asbury Park, secretary, and William H. Seward, Orange, treasurer.

NEW YORK

Increased Fees in Relief Cases.—The Medical Society of the County of Erie was instrumental in having approved on June 14 an increase in fees for relief cases. The Erie County Board of Social Welfare voted the action, effective November 1, in conformance with the society's recommendations.

Prevalence of Rabies.—Quarantine of all dogs in Rochester and seven adjoining townships was put into force July 1 as a result of a certification of the existence of rabies issued June 26 by Dr. Edward S. Godfrey Jr., Albany, state commissioner of health, newspapers reported. Two cases of rabies in dogs reported within the week prompted the order. Positive diagnosis of rabies in a dog in Flushing, Queens, was formed by the New York City Department of Health, it was reported June 29, the first to be reported in the city since February and the first occurrence of the disease in the borough of Queens since August 1941.

New York City

Columbia to Receive Fund for Cancer Research.—On termination of a residuary trust set up under the will of Mrs. Edith Dunshee Converse, who died June 21, Columbia University will receive one half of the principal, the income to be used for the maintenance and equipment of a laboratory for research in the field of malignant diseases. The fund will be known as the "Edith Dunshee Converse Fund," newspapers report.

Student Prizes Awarded.—At the one hundred and ninety-first commencement of Columbia University, June 5, prizes to seniors included the Janeway prize to J. P. Cole for the highest marks in efficiency and ability. The Harold L. Meierhof Memorial Prize for the best work in pathology during the year went to George Lally Curran. Virginia C. Nichols was given the Dr. William Perry Watson prize in pediatrics, an award going to the student who has been in attendance on the regular course of instruction for at least two years and who has shown the most notable work in the study of the diseases of infants and children. Another feature of the commencement exercises included the presentation of the honorary degree of doctor of science to Edwin J. Cohn, Ph.D., professor of biochemistry, Harvard Medical School, Boston, and to Dr. Herbert S. Gasser, director of the Rockefeller Institute for Medical Research.

NORTH CAROLINA

David Young Named Superintendent of Mental Health.—Dr. David A. Young, assistant professor of psychiatry and neurology, University of Utah School of Medicine, Salt Lake City, has been appointed general superintendent of mental health for the four state hospitals of North Carolina, a newly created position. The appointment will be effective September 1. In making the selection, five candidates for the position were chosen to familiarize themselves with the position and, during the course of their study, their expenses were paid. The five considered were, in addition to Dr. Young, Colonel Lloyd J. Thompson, M. C., Lieut. Col. Walter E. Barton, M. C., Lieut. Col. Malcolm J. Farrell and Dr. Gaylord P. Coon, Boston. The new superintendent is to coordinate the work of the four state institutions in order that better medical and mental care may be available. The position was authorized by the 1943 general assembly and never filled. It was, however, given new emphasis by the 1945 assembly, which also set up a new hospitals board of control (THE JOURNAL, June 16, p. 532). The governor, following his appointments to the new board, also appointed a twelve man advisory commission to assist the board with Dr. Hubert B. Haywood, Raleigh, as chairman. The proposed program of better care includes a plan to buy a post hospital at Camp Sutton, Monroe, from the United States government, since it has been abandoned by the army. This, if carried out, will be used to take care of about 1,000 of the senile arteriosclerotic group in the other hospitals, freeing beds for the care of patients for whom there may be some hope of a cure.

OHIO

Fifty Years of Practice.—Physicians who have recently completed fifty years in the practice of medicine include Drs. Samuel L. Bernstein, Cleveland; Albert J. Bausman, Piqua, and Dr. Frank B. Gregg, Wellington.

Graduate Training for Returning Veterans.—On July 1 the Ohio State University College of Medicine, Columbus, launched a plan for postgraduate training designed primarily for returning veterans and other physicians who may wish to participate. Those who take the course will be required to spend full time in the university hospital or affiliated institutions of the medical school for a period of not less than two weeks nor longer than three months and will be under the immediate supervision of one of the members of the faculty whom they shall select and who shall serve as a counselor. Additional information may be obtained from Dr. Bruce K. Wiseman, Kinsman Hall, Ohio State University, Columbus 10.

Charles McKhann Named Professor of Pediatrics at Western Reserve.—Dr. Charles F. McKhann, assistant to the president in charge of research, Parke, Davis & Company, Detroit, has been named professor of pediatrics at Western Reserve University School of Medicine and director of pediatrics at University Hospitals, Cleveland. He succeeds Dr. Henry J. Gerstenberger as professor of pediatrics at Western Reserve and director of Babies and Childrens and Rainbow hospitals. Dr. Gerstenberger will become professor emeritus of pediatrics beginning with the next school year. The appointment became effective as of July 1, but Dr. John A. Toomey will remain as acting director of University Hospitals until September 1 and will also continue as professor of clinical pediatrics and contagious diseases at the school of medicine and in charge of the departments of contagious diseases at the university and city hospitals. Dr. Toomey was appointed acting director of pediatrics at University Hospitals when Dr. Gerstenberger was granted a leave of absence in July 1944 to devote most of his time during the next five or six years preparing a mass of clinical and scientific data for publication and writing a history of the Babies and Childrens Hospital and its predecessors (THE JOURNAL, Aug. 19, 1944, p. 1152). Dr. McKhann graduated at the University of Cincinnati College of Medicine in 1923. He served in various capacities at Harvard Medical School, Boston, and the Harvard School of Public Health from 1923 to 1940, when he went to the University of Michigan Medical School, Ann Arbor, as professor of pediatrics and communicable diseases. For a year in 1935 he was visiting professor of pediatrics at Peiping Union Medical College on a grant from the Rockefeller Foundation.

OKLAHOMA

Public Relations Program Approved.—The Oklahoma State Medical Association has activated a public relations program encompassing public and postgraduate education, postwar planning and plans to foster closer unity of county medical societies. The project designed for public education will use the press, radio, motion pictures and public speakers to present the importance of scientific medicine to the public. Postgraduate activities will include cooperation with a project now under consideration by the University of Oklahoma School of Medicine, Oklahoma City. The state department of public health and the state association will cooperate in the postwar program

to be of benefit of doctors returning from service. The interest of the state association in its county medical societies will be continued, and service will be expanded to assist the local units in carrying out service to the public.

New Board of Health Formed.—On June 15 the governor appointed the new nine member state board of health, created under the recently enacted house bill number 77, which stipulated that the new board be composed of a representative from each congressional district and one from the state at large, five to be members of the Oklahoma State Medical Association. The board members are:

Dr. Charles R. Rountree, Oklahoma City, board member at large, nine year term.
A. G. Reed, osteopath, Tulsa, first district, six year term.
Dr. Charles Edgar White, Muskogee, second district, five year term.
Dr. Tracey H. McCarley, McAlester, third district, three year term.
Dr. Catherine F. T. Brydia, Ada, fourth district, one year term.
Mr. Bert Loy, hospital administrator, Oklahoma City, fifth district, seven year term.
Mr. William F. Schumacher, engineer, Lawton, sixth district, two year term.
Dr. Victor C. Tisdal, Elk City, seventh district, eight year term.
Fred Seids, D.D.S., Perry, eighth district, four year term.

Officers are Dr. Rountree, chairman, Dr. White, vice chairman and Mr. Loy, secretary. At the organization meeting, June 22, Dr. Grady F. Mathews, Oklahoma City, was unanimously voted to continue as state health commissioner.

PENNSYLVANIA

District Meetings.—The annual meeting of the Eighth Councilor District of the Medical Society of the State of Pennsylvania met June 27 in Meadville. Among the speakers were Drs. Bernard Fisher, Pittsburgh, on "Penicillin vs. Sulfonamide Therapy—A Clinical Evaluation" and William Bates, Philadelphia, "Early Diagnosis of Carcinoma of the Rectum." Drs. Thomas O. Glenn, Bradford, and Franklin G. Haines, Warren, were presented with testimonials in recognition of their completion of fifty years in the practice of medicine. The Ninth Councilor District held its annual meeting in Punxsutawney June 28. Addresses were given by Dr. Fisher, Dr. John P. Henry, Pittsburgh, on "Thrombophlebitis: Its Modern Treatment" and Dr. Charles J. Barone, Pittsburgh, "Obstetrics in General Practice." Members honored for their completion of fifty years in the practice of medicine were Drs. Joseph J. Schultis, Butler; Howard B. Buterbaugh, Indiana; William A. Simpson, Indiana; Harry B. King, Reynoldsville, and Rose M. Dunn, Franklin.

Philadelphia

Alexander Wiener Receives Alvarenga Prize.—On July 14 the College of Physicians of Philadelphia is awarding the Alvarenga Prize to Dr. Alexander S. Wiener, serologist to the office of chief medical examiner of New York City, in recognition of his work on the various types of Rh factors and on their genetic transmission. On October 3 Dr. Wiener will give the Alvarenga Lecture before the college and the Philadelphia County Medical Society on "Rh Blood Factors in Clinical Medicine." The Alvarenga Prize was established by the will of Pedro Francisco deCosta Alvarenga, Lisbon, Portugal, an associate fellow of the college of physicians, "to be awarded annually by the college of physicians on each anniversary of the death of the testator, July 14, 1883." The college usually makes this award for significant published work and invites the recipient to deliver an Alvarenga Lecture before the college.

TENNESSEE

Dr. Burch Retires.—Dr. Lucius E. Burch on July 1 retired as professor and chairman of the department of obstetrics and gynecology at the Vanderbilt University School of Medicine, Nashville. Dr. Burch, who graduated at Vanderbilt in 1896, joined the faculty in 1902 as professor of gynecology. He was dean of the school from 1914 until he retired to become head of the department of obstetrics and gynecology.

PUERTO RICO

Status of Veterans Facilities.—Dr. Jaime Serra Chavarry, head of the insular office of the veterans administration in San Juan, left for Washington recently to confer with General Omar N. Bradley, newly appointed veterans administrator, on plans for the expansion of the veterans administration in Puerto Rico and possibly will urge that the federal government build a veterans' hospital on the island, it is reported. Under the present setup veterans are hospitalized by the administration in private clinics and hospitals, which receive payment from the federal government. These clinics and hospitals, numbering fourteen in all, have 1,000 beds available for veterans and a minimum of 100 beds for emergency cases at all times, which is considered insufficient for the large number of veterans that will return to this island after final defeat of the Japanese. The construction of a veterans hospital in Puerto Rico, however, would release 1,100 beds to the general public, in addition to providing the type of care and attention that federal supervision would guarantee. Present arrangements are inadequate. Simultaneously, the increase in requirements for the general public in island hospitals will add in the next three or four years to the burden of providing proper hospitalization and medical attention for the population.

GENERAL

Journal Honors Physicians.—A recent issue of the *Review of Gastroenterology* was dedicated to Drs. Samuel Weiss, New York, and Charles W. McClure, Boston, in honor of their sixtieth birthdays. Dr. Weiss has been editor of the *Review* since March 1934. Dr. McClure is a charter member of the National Gastroenterological Association and helped to organize the Boston chapter, of which he is secretary-treasurer.

Quinacrine Again Under Allocation Control.—Because of increased American and allied military requirements for quinacrine, popularly called atabrine, in line with the redeployment of troops to the Pacific areas, the War Production Board June 19 placed the chemical under allocation control of schedule III of order M-300, the general chemicals allocation order. Quinacrine, used for the treatment of malaria, was originally placed under allocation in April 1943, when increased military requirements for the chemical, to be used as a substitute for quinine, made the available supply inadequate to meet demands. However, lessened military demands later in the war made it possible to remove allocation controls in January of this year. It will be necessary to increase production of the drug in order to meet all requirements fully. With controlled distribution, adequate supplies of quinacrine will be assured for civilian use in malarial regions of the United States.

Form Corps of Poliomyelitis Emergency Volunteers.—The National Foundation for Infantile Paralysis is organizing a nationwide program to form and train a corps of poliomyelitis emergency volunteers to assist physicians, physical therapists and nurses in areas where infantile paralysis epidemics occur. The new corps will be called "PEVS." The initial phases of the program provide only for instruction in those areas where qualified teaching personnel, institutional facilities for the care of poliomyelitis victims and actual infantile paralysis cases exist or are anticipated during the coming year. If an outbreak occurs in an area where the volunteers have not been organized and trained, the foundation will be prepared to give emergency training assistance through emergency courses. The course, designed for eight lecture and demonstration classes of two hours each, will be scheduled for local convenience. The volunteers will be organized through the women's committees in charge of Miss Elaine Whitelaw, director of women's activities of the national foundation.

Social and Environmental Factors in Medicine.—The Milbank Memorial Fund has given a grant to finance a study by the Association of American Medical Colleges in cooperation with the American Association of Medical Social Workers on the teaching of the social and environmental factors in medicine. A committee of twenty-five physicians and medical social workers who are engaged in this teaching has been formed to direct the study, under the name of the Joint Committee on the Teaching of the Social and Environmental Factors in Medicine. The co-chairmen are Dr. Jean A. Curran, dean, Long Island College of Medicine, Brooklyn, and Miss Eleanor E. Cockerill, associate professor of social case work at the School of Applied Social Sciences, University of Pittsburgh. A centrally located project subcommittee has been set up under the chairmanship of Dr. Jonathan E. Rhoads, assistant professor of surgical research and acting director of the Harrison Department of Surgical Research, University of Pennsylvania School of Medicine, Philadelphia. The executive secretary of the study is Miss Harriett M. Bartlett, 49 Fruit Street, Boston 14. It is the aim of the study to bring together and analyze the experience of the group of medical schools in introducing students to the social and environmental components in medicine. Visits to selected centers will be made by members of the committee. The study is expected to last through 1945, at the end of which time a report summarizing the findings will be prepared.

Blue Cross Opens National Enrolment Office.—To assist in the enrolment of employees of national firms with plants or branch offices located in areas served by two or more Blue Cross hospital and medical prepayment organizations, the Blue Cross Plans of the United States will open a national enrolment office on July 16 in New York. The enrolment office will be an activity of the American Hospital Association's hos-

pital service plan commission, which coordinates the program of the Blue Cross Plans serving forty-three states, seven Canadian provinces and Puerto Rico, Clarence Rufus Rorem, Ph.D., Chicago, director, said in making the announcement. Headquarters of the national enrolment office will be located at 370 Lexington Avenue, room 1014, New York. The enrolment director will be Frank Van Dyk, who has served the New York City Blue Cross Plan for the past ten years and who will continue as vice president in charge of enrolment for Associated Hospital Service of New York in addition to his new duties. Mr. Van Dyk will represent the various Blue Cross Plans in their presentation of a uniform program to national firms, but each local state and community organization will conduct the actual enrolment and pay hospital bills for the local employees of a national firm or organization. As a further encouragement to national enrolment, the Blue Cross Plans have agreed to enroll the branch office or branch store employees of a national firm even though the number of employees may not meet the minimum group requirements of the enrolling plan. Blue Cross Plans have agreed also to accept transfers of membership when the employee of a nationally enrolled firm moves. Transfer of membership of the employee's family is also included.

Prevalence of Poliomyelitis.—Reports of cases of poliomyelitis for the week ended June 30 have been received from the division of public health methods, U. S. Public Health Service, as follows:

	Week Ended June 30, 1945	Week Ended July 1, 1944
New England		
Maine	0	0
New Hampshire	0	1
Vermont	0	0
Massachusetts	2	0
Rhode Island	0	0
Connecticut	1	0
North Atlantic		
New York	16	25
New Jersey	5	2
Pennsylvania	1	6
East North Central		
Ohio	5	6
Indiana	3	0
Illinois	2	2
Michigan	0	0
Wisconsin	0	2
West North Central		
Minnesota	1	5
Iowa	1	0
Missouri	2	1
North Dakota	0	0
South Dakota	0	0
Nebraska	0	0
Kansas	1	1
South Atlantic		
Delaware	1	0
Maryland	1	1
Dist. of Columbia	3	0
Virginia	5	6
West Virginia	2	1
North Carolina	5	83
South Carolina	8	2
South Atlantic—Cont.		
Georgia	1	2
Florida	1	6
East South Central		
Kentucky	3	29
Tennessee	6	1
Alabama	7	1
Mississippi *	..	3
West South Central		
Arkansas	1	4
Louisiana	1	4
Oklahoma	3	2
Texas	54	5
Mountain		
Montana	0	0
Idaho	0	0
Wyoming	0	0
Colorado	0	1
New Mexico	0	0
Arizona	0	0
Utah	0	0
Nevada	0	0
Pacific		
Washington	0	0
Oregon	1	5
California	12	13
Total	155	220
First 26 weeks:		
1945 and 1944	1,270	1,003
Median, 1940-1944	776	

* No report received for current week.

LATIN AMERICA

Health Activities in Latin America.—*Visitors to the United States.*—Dr. Manuel Picco, Buenos Aires, Argentina, is to specialize in orthopedics at the Lahey Clinic, Boston, on a travel grant awarded by the Institute of Inter-American Affairs.——Dr. Victor Grossi, chief of the public health office of Valparaiso, Chile, has gone to the United States to carry on a tour of health and sanitation programs in several states.

Society News.—Dr. Dante Pazzanese has been chosen president of the newly created Sociedade Brasileira de Cardiologia, with headquarters in Campinas, São Paulo, Brazil. Other officers include Drs. Adriano de Azevedo Pondé, vice president, and Jose de Proenca Pinto de Moura, secretary. Dr. Leovigildo Mendonca de Barros is editor of the *Arquivos de Cardiologia*, the official journal of the society.

Personal.—Dr. Peter A. Clearkin, government bacteriologist of British Guiana, recently was the recipient of a decoration from King George VI of England for his work in 1944.——Dr. Antonio Peña Chavarría, director of the Hospital San Juan De Dios, San José, Costa Rica, has been granted a fellowship from the John and Mary R. Markle Foundation, through the Association of American Medical Colleges, according to *Tropical Medicine News*. It was to become effective early in May and will be utilized in visits to various medical centers in the United States. The fellowship was granted Dr. Peña in recognition of the great services rendered by him to instructors from medical schools of the United States and Canada, who for the last eighteen months have been gaining practical experience in tropical medicine in San José under his direction.——Eric G. Ball, Ph.D., associate professor of physiologic chemistry at Harvard Medical School, Boston, is giving a series of lectures at the School of Medicine of the University of Brazil in Rio de Janeiro, where he will direct research in cellular respiration, according to *Science*. His trip is under the joint auspices of the Brazilian government and the department of state of the United States.——Brig. Gen. Henry C. Dooling, M. C., who was on a thirty day mission in the battle areas of the Mediterranean theater, has returned to his activities as chief health officer of the Panama Canal. While in Italy, General Dooling met Major Gen. Morrison C. Stayer, M. C., who preceded him as chief health officer of the Panama Canal. Col. Albert R. Dreisbach, M. C., acted as chief in General Dooling's absence.

Division of Child Welfare in Rio Branco.—A division of child welfare has been recently established in the territory of Rio Branco, Brazil, according to the *Child*. This division will engage in preventive and curative work under the general supervision of the National Children's Bureau in Rio de Janeiro. The present plans provide for medical and dental care and improvement of nutrition for all children and youth in the municipalities. The territory has been divided into fifteen districts, in each of which will be established a maternity home, a milk station for children, a day nursery and a kindergarten.

Smallpox Vaccination of Civilian Residents.—On June 1 the health department of the Panama Canal started smallpox vaccination of about 300,000 civilian residents in the Canal Zone and the cities of Panama and Colon. Authority for the undertaking is derived from board of health ordinance number 5, approved in 1915, which provides that all persons living in these communities must submit to the vaccinations at intervals of not more than five years. A similar campaign was conducted in 1940.

Argentina's Plan for Health.—The National Health Department, an agency of the Ministry of the Interior, which is said to dominate unrestrictedly the health and sanitation activities in Argentina, proposes, through a national sanitary plan and enforcement measures now being formulated, to carry on an intensive drive against cancer, cholera, bubonic plague, heart diseases, pneumonia, yellow fever, smallpox, exanthematous typhoid, diphtheria, mumps, scarlatina, whooping cough, lethargic or epidemic encephalitis, infantile paralysis, grip, tuberculosis, leprosy, rabies and trachoma.

Conference on Tropical Dermatology.—A course on tropical dermatology will be conducted in Mexico City August 6-18 under the direction of Dr. Fernando Latapi, professor of dermatology, Universidad Nacional Facultad de Medicina, Mexico, D. F., and with the cooperation of Secretaria de Salubridad y Asistencia Publica. Applications to take the course should be sent to Dr. Latapi, Zacatecas 220-6 Mexico, D. F., Mexico. Additional information may be obtained from Dr. Leon Goldman, University of Cincinnati College of Medicine, Cincinnati 1. The program, prepared at the request of Dr. Howard Fox, New York, has been made up especially for American dermatologists and will include a summary of general information, the presentation of clinical cases and laboratory demonstrations, such as bacteriology, parasitology, mycology and histopathology:

Dr. Jesus Gonzalez Urueña, Tropical Characteristics of Mexican Dermatology.
Dr. Salvador Gonzalez Herrejón, Pinta.
Dr. Manuel Martinez Baez, Onchocerciasis.
Dr. Julio Bejarano, Syphilis.
Dr. Latapi, Leprosy.
Dr. Antonio Gonzalez Ochoa, Mycosis and Tinea Capitis.
Dr. Jorge Millan Gutierrez, Leishmaniasis.
Dr. Oswaldo S. Arias, Lymphogranuloma Venereum.

FOREIGN

Personal.—Dr. John A. Nixon, Bristol, was appointed Dr. Alexander Black lecturer for 1945 for the Royal College of Physicians of Edinburgh.

National Institute of Physiology in China.—*Science* reports that equipment for a National Institute of Physiology in China, devoted entirely to the study of developmental physiology, is now being purchased in the United States by the future director of the institute, Dr. Shu Chu Shen, who is working in the Highpolymer Research Bureau of the Polytechnic Institute of Brooklyn. Dr. Shen is in the United States as a representative of the ministry of education of the Chinese government. It is planned to establish the institute in Shanghai after the war, since it is advisable to have it near a seaport. One of the first projects will be the investigation of the nutritional status of Chinese children with a view to improving the content of foods with essential minerals and vitamins.

Foreign Letters

LONDON

(From Our Regular Correspondent)

June 9, 1945.

The Treatment of Advanced Starvation

The conditions in German prison camps and in occupied countries have brought to the front the problem of the treatment of advanced starvation. At the Royal Society of Medicine Dr. H. E. Magee opened a discussion on this subject, particularly on the use of protein hydrolysates. He worked for several years on the physiology of absorption and found that as fasting continues there is a progressive diminution in the absorptive powers and protective functions of the intestinal mucosa. The columnar epithelium is progressively disorganized, exposing the intestine to irritation by undigested foods with resultant diarrhea. Parenteral feeding, by injection of amino acids to reconstruct the mucosa, is indicated. These should be used by the body as building materials but in starvation are apt to be broken down and used for energy. To protect them it is necessary to give glucose and B vitamins, which enable the body to metabolize glucose.

Dr. Hugh S. Stannus said that the conditions in starvation for which protein hydrolysate therapy had been introduced made a complex picture of many unknowns. If the patient could swallow, digest and absorb the requisite protein, this might be supplied in some suitable form, such as reconstituted dried skim milk powder by mouth or, if he could not swallow, by nasal tube feeding. But if he was unable to digest, protein hydrolysate should be given by mouth or by gavage and if he could not swallow, digest or absorb, resort must be made to intravenous administration. But this conception had been shaken by the case of a repatriated prisoner in the last stages of starvation who had difficulty in taking his milk diet. The case seemed to demand intravenous hydrolysates, but none were available. He was therefore given glucose-saline intravenous therapy, a crude liver extract parenterally and teaspoon feeding with powdered liver extract. The response was dramatic, and the same result was obtained in another case.

Dr. Janet Vaughan, who was one of a small team sent out by the Medical Research Council to test the various methods of feeding in the Belsen camp, described the horrible conditions she found there. She first discussed intravenous therapy. Five patients were given amigen, which they took well, with no reaction. Four did well, but the fifth showed no improvement. The workers had no doubt that for intravenous therapy serum was preferable to hydrolysates. The explanation was that with it there was much more protein and relatively little fluid.

Mass Radiography in the Early Detection of Pulmonary Tuberculosis

The Medical Research Council has published a report on the results obtained by mass miniature radiography in the early detection of tuberculosis of the lungs. A survey of 23,000 persons from two factories, a large office group and a mental hospital, all in greater London, was conducted. Leaving out the mental hospital, because tuberculosis has long been known to show a higher incidence than the average in such institutions, interest centers on the early detection of disease among the general working population. The figures for the two factories and the office group were similar: between 1 and 1.5 per cent newly discovered tuberculous lesions. About a fourth of the persons affected were advised to leave work immediately for institutional treatment. The rest required outpatient observation while remaining at work. If the persons examined can be taken as a fair sample for the rest of the country, these figures mean an immediate temporary loss of 3 or 4 per thousand and some adjustment of work of 10 per thousand remaining under supervision. The final diagnosis was not made on a miniature film alone. About 6 per cent of persons were asked to return for a full size film and about 2.5 per cent for a medical interview.

Two Benefactors of Blinded Prisoners of War in Germany

Major Charteris, the Liverpool ophthalmic surgeon who twice declined repatriation in order to continue his treatment of men in German prison camps, was welcomed at a luncheon in London, which was presided over by Sir Ian Fraser, chairman of St. Dunstan's (the institute for blinded soldiers and sailors). Major Charteris was captured in Greece in 1940 and sent to Germany, where his captors soon recognized his skill in treating eye casualties. Twenty-five blind ex-prisoners of war, escorted by their wives or fiancées, were present at the luncheon. Another benefactor of the blinded prisoners, Lord Normanby, also was thanked. He was severely wounded, though not blinded, in the battle of France and while in a German hospital became interested in the blinded prisoners there. He taught himself braille from a book he found in a salvage dump and then instructed blinded soldiers how to read, thus establishing the camp instructional school, which developed with the help of materials sent by the British Red Cross.

BRAZIL

(From Our Regular Correspondent)

São Paulo, May 28, 1945.

Campaign Against Trachoma

Besides the state of São Paulo, the third most important focus of trachoma in Brazil, where there is a special service of the state health department to combat the disease, two important areas of the highest prevalence of trachoma exist in Ceará, a northern state, and in Paraná, a southern state, where the efforts against that scourge have not yet been organized on a practical basis. In some districts of the state of Paraná a previous survey of a good sample of the population disclosed that an average of 10 per cent of the school children and 30 per cent of the adult rural population presented the disease. For this reason the National Department of Health has founded in the latter two states, in cooperation with the local authorities, several centers of treatment and control of the disease under the supervision of Dr. Herminio B. Conde, an able ophthalmologist with an extensive knowledge of the problem of trachoma. Some particular data are now available concerning the antitrachoma work during the first quarter of this year. Of 23,144 persons examined, 1,288 new cases have been discovered, for which 10,519 dressings and 20,866 instillations of collyria have been done, and 26,815 tablets of sulfonamide preparations have been distributed. Clinical cure was obtained in 221 cases. Among these trachomatous persons an average of 2 per cent were blind in both eyes, 6 per cent were blind in one eye, 29 per cent had lost 5/10 of the ocular acuity, 37 per cent had lost 3/10 of the acuity and 26 per cent had normal vision. This month a new survey is just beginning which will cover the great valley of the São Francisco river, which flows from the south to north through central Brazil and is the axis of large migrations of population that link the northern and the southern areas of high prevalence of trachoma.

Prolapses of the Uterus and Cancer

All medical publications agree in finding exceptional the association between prolapse and cancer of the cervix of the uterus. Recently Dr. Licinio Dutra published a paper including 3 well documented cases with another 5 cases taken from Brazilian gynecologists. After reviewing the different theories which have been formulated to explain the coincidence of these

two disorders Dr. Licinio Dutra draws the following conclusions: "The poor blood and lymph circulation associated with uterovaginal prolapse, the atrophy of the mucous membrane and of the endocervical and endometrial glands and the rarity of inflammatory manifestations of the irritative type might explain why uterine prolapse and cervical cancer so seldom coincide, together with the excessive cornification and the altered epithelium of the mucous membrane of the cervix and vagina, which reduce the possibility of cancer in uterine prolapse."

Brazilian Oranges

Much research is being aided by grants from the Fundos Universitários de Pesquisas para a Defesa Nacional. Experiments have been performed at the Department of Physiology of the Faculdade de Medicina de São Paulo by Prof. Franklin de Moura Campos to study the nutritive value of certain varieties of Brazilian oranges. It was found that Brazilian oranges are poor in calcium salts. Ascorbic acid and thiamine were found in large amounts. Ascorbic acid was determined by a photoelectric colorimeter (Klett-Sumerson) and vitamin B_1 by the rat growth method devised by Miller.

The following conclusions may be drawn from Professor Moura Campos's investigations:

1. Brazilian oranges are poor in calcium salts, 0.016 Gm. per hundred grams being found on the average.

2. Some Brazilian oranges (Lima, Pera) are rich in ascorbic acid. Lima oranges presented an average of 55.48 mg. per hundred grams, Pera oranges 31.22 mg. per hundred grams.

3. Seleta and Pera oranges are rich in vitamin B_1. Both are given as the only source of thiamine that either prevented or cured beriberi.

4. Daily doses of 1 cc. of Seleta orange juice showed preventive action; doses of 2 cc. cured vitamin B_1 deficient animals.

5. Pera orange juice also was active.

Death of Dr. Adolph Lindenberg

Dr. Adolph Lindenberg, a leading dermatologist of São Paulo and a great figure of Brazilian medicine, died recently at an advanced age. Dr. Lindenberg was the founder of modern dermatology in São Paulo. He was a true representative of the great period of parasitologic investigation in dermatology, in which he became famous in Brazil as well as in all South America. Beginning with the first parasitologic identification of leishmaniasis in Brazil in 1909, he made in 1911 extensive researches on the subject of sporotrichosis, then a new disease described for the first time by A. Lutz in Brazil. The careful study of a patient affected with a mycetoma of the knee led Lindenberg to discover a new species of Actinomyces—Discomyces brasiliensis. He was one of the pioneers of the idea of the extraordinary clinical polymorphism of neotropical blastomycosis. One of the last subjects that interested Dr. Lindenberg in his parasitologic investigations in dermatology was pemphigus foliaceus ("wild fire"), the cause of which is still an engima. Among the several distinguished disciples of the dermatologic school which Lindenberg created in São Paulo are Dr. A. Martins de Castro and Dr. N. Rossetti.

Brief Items

Dr. Eurico Rangel, director of the Statistical Division of the Serviço de Biometria Medica, died recently at the age of 59. Dr. Rangel studied medical biometry and statistics at the School of Hygiene and Public Health of the Johns Hopkins University in 1925-1926 and was director of the Vital Statistics Bureau of the National Department of Health at Rio de Janeiro from 1933 to 1940.

On June 18-21 the annual meeting of the Brazilian Heart Association will be held. The medicosocial care of cardiac patients, the functional recuperation of such patients and neurocirculatory asthenia are the principal topics to be discussed. The organization committee includes Drs. Genival Londres and Oscar Ferreira Jr. of Rio de Janeiro and Drs. Dante Pazzanese and L. Mendonça Barros of São Paulo.

Drs. Guilherme M. Hautz, Raymundo B. Menezes and Wilson G. Santiago have been appointed professors of the Brazilian Army Medical School.

A modern hospital has been inaugurated in the state of Minas Gerais at Rio Preto (population 18,000). The fund for the erection of the hospital and for its maintenance has been raised from the population of the small city and the neighboring country.

The annual meeting of the Brazilian Association of Dermatology and Syphilography will be held at Belo Horizonte, state of Minas Gerais, on September 24-26. The principal subjects to be discussed are blastomycosis and the modern treatment of syphilis.

Dr. Alvaro Bahia, director of the division of child hygiene of the department of health of the city of Salvador, state of Bahia, left a few days ago for the United States, where he will study some organizations devoted to child welfare.

Dr. J. P. Azevedo Sodré, surgeon of the Municipal Emergency Hospital of Rio de Janeiro, has been elected a member of the National Academy of Medicine.

Marriages

WILLIAM BOYKIN LYLES JR., Spartanburg, S. C., to Miss Barbara S. Spencer of Dursley, Gloucestershire, England, March 28.

DAVID A. CLEVELAND, Milwaukee, to Mrs. Mary Macklin Stephens of Beverly Hills, Calif., in Riverside, Calif., February 26.

CHARLES AUGUST RENTROP JR., Germantown, Tenn., to Miss Marion Henrietta Meyn of Wallkill, N. Y., in Newburgh, N. Y., June 2.

MORRIS RAPPAPORT, Ellenville, N. Y., to Miss Judith Helen Preminger of Perth Amboy, N. J., March 18.

HENRY RANDALL THOMAS, Montgomery, Ala., to Miss Patricia Jane Piper of Rochester, Minn., May 26.

ROSS SIMONTON MCELWEE JR., Statesville, N. C., to Miss Doris Edgar in Kingston, N. Y., June 2.

NEWELL JEROME GRIFFITH, Tuckahoe, N. Y., to Miss Florrie Margaret Collins of Perry, Fla., June 2.

LOGAN UNDERWOOD MEWHINNEY, Holland, Texas, to Dr. RUTH ISADORA ALLEN of Dallas in May.

ALBERT F. TATUM, Tuscaloosa, Ala., to Miss Mary Nell Routledge of Birmingham, May 18.

HERBERT WINSTON FROSTICK to Miss Jean Caroline Wall, both of Charlotte, N. C., recently.

ROBERT J. ATWELL, Chillicothe, Ohio, to Miss Paula Mozelle Mitchell in Dayton, April 28.

HOWARD J. OHL, Lordsburg, N. M., to Miss Mary C. Shores of Union Star, Mo., April 3.

DOUGLAS T. LINDSAY, Minneapolis, to Miss Nelda Kanne of Faribault, Minn., March 26.

MILTON SALASKY, Norfolk, Va., to Miss Shirley Greenberg of San Francisco, May 19.

MACK RAYBURN to Mrs. Virginia Wilson Elam, both of Owensboro, Ky., April 6.

LORIN L. FOWLER, Marion, Ill., to Mrs. Lulu Caplinger of Downey, Calif., May 4.

MICHAEL J. LARKIN to Miss Helen M. Carroll, both of Trenton, N. J., June 20.

MANSON MEADS to Dr. HELEN WHEELER BELDING, both of Boston, May 26.

MARTIN SCHWEITZER to Miss Dorothy R. Chess, both of New York, June 9.

IRVING M. GREENBERGER to Miss Letty London, both of New York, June 3.

Deaths

William Hans Henry August Vogt ✠ St. Louis; Missouri Medical College, St. Louis, 1897; joined the faculty of St. Louis University School of Medicine as instructor in gynecology and obstetrics in 1919, holding that position until 1924; assistant professor from 1924 to 1929 and associate professor from 1929 to 1933, when he became professor of gynecology and obstetrics and director of the department; instructor in gynecology and obstetrics at the Washington University School of Medicine from 1910 to 1915; specialist certified by the American Board of Obstetrics and Gynecology, Inc.; member of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Southern Medical Association and the Central Association of Obstetricians and Gynecologists; past president of St. Louis Medical Society; served at various times on the gynecologic and obstetric staffs of Lutheran Hospital, City Sanitarium, City Infirmary, St. Louis Maternity, St. Luke's, St. John's and St. Louis City hospitals, St. Mary's Group of Hospitals and Deaconess Hospital and Home; since 1933 member of the advisory staff of St. Mary's Infirmary; died in Atlantic City, N. J., June 17, aged 68, of coronary thrombosis.

Henry Joseph Frederick Wallhauser ✠ Mount Bethel, Pa.; University of the City of New York Medical Department, 1888; specialist certified by the American Board of Dermatology and Syphilology; past president of the Essex County (N. J.) Medical Society; member of the New Jersey Dermatological and Manhattan Dermatological societies; formerly medical director of Newark City Dispensary; consulting dermatologist to the Mountainside Hospital, Montclair, N. J., Overlook Hospital, Summit, N. J., Essex County Hospital for Contagious Diseases, Belleville, N. J., St. Mary's Hospital, Orange, N. J., and Lutheran Memorial Hospital, Crippled Children's Hospital, Babies' Hospital, Presbyterian Hospital, Newark City Hospital and the Hospital of St. Barnabas and for Women and Children, Newark, N. J., where he died May 5, aged 80, of arteriosclerosis and myocardial degeneration.

Oscar Francis Cox, Brookline, Mass.; Tufts College Medical School, Boston, 1914; professor of clinical urology at his alma mater and associate professor of medicine at the Boston University School of Medicine; served overseas during World War I; member of the subcommittee on venereal diseases of the National Research Council; secretary of the American Neisserian Medical Society; member of the American Medical Association; a director of the Massachusetts Society for Social Hygiene; director of the division of genitourinary diseases at the Massachusetts Memorial Hospital, Boston; chief of the genitourinary clinic of the Boston Dispensary; chairman of the advisory committee on venereal disease control of the Massachusetts Department of Public Health; died June 3, aged 57, of primary carcinoma of the lung.

John Pascal Sawyer, Cleveland Heights, Ohio; Western Reserve University Medical Department, Cleveland, 1886; since 1932 professor emeritus of therapeutics and clinical medicine at his alma mater, where he had served on the faculty in various capacities for many years; specialist certified by the American Board of Internal Medicine; member of the American Medical Association, American Gastro-Enterological Association and the Cleveland Academy of Medicine; fellow of the American College of Physicians; a trustee of the Cleveland Medical Library Association; emeritus chief of staff at St. Vincent Charity Hospital, Cleveland, where he died June 17, aged 83, of perforated stomach ulcer and terminal pneumonia.

Harold Glen Stevenson, Utica, N. Y.; University of Toronto Faculty of Medicine, Toronto, Ont., Canada, 1920; on the staff of the Oneida County Tuberculosis Sanatorium (Broadacres); at one time superintendent of the Berks County Sanatorium in Reading, Pa.; formerly on the staffs of the Eagleville Sanatorium for Consumptives, Eagleville, Pa., Montgomery Sanatorium, Amsterdam, Pennsylvania State Sanatorium, South Mountain, Niagara Sanatorium in Lockport, Loomis Sanatorium, Loomis, and the Neversink Sanatorium, Reading, Pa.; died May 4, aged 49, of chronic arthritis and myocardial failure.

George Ollie Allen, Marietta, Ga.; Southern Medical College, Atlanta, 1893; member of the American Medical Association; past president of the Cobb County Medical Society; served during World War I; while a resident of Fargo served as physician and surgeon for the Southern Railway Company; on the staff of the Marietta Hospital; member of the Marietta Rotary Club; died May 26, aged 73, of coronary thrombosis.

John Andrews, Grant City, Mo.; Rush Medical College, Chicago, 1892; on the courtesy staff of the Missouri Methodist Hospital, St. Joseph, where he died May 16, aged 79, of hypertensive and arteriosclerotic heart disease.

Guy Frank Arnold, Washington, D. C.; Baltimore Medical College, 1900; died May 26, aged 68, of gastric hemorrhage and cerebral thrombosis.

Mary Lantz Austin, Gallipolis, Ohio; Ohio Medical University, Columbus, 1904; for many years on the staff of the Ohio Hospital for Epileptics; died in the Holzer Hospital May 21, aged 78, of cerebral and generalized arteriosclerosis and chronic arthritis.

Clarence H. Barber, Grand Rapids, Mich.; the Hahnemann Medical College and Hospital, Chicago, 1891; member of the American Medical Association; on the staff of the Michigan Veterans' Facility, where he died May 18, aged 75, of coronary thrombosis and pulmonary edema.

Arthur J. Behrendt, Chicago; College of Physicians and Surgeons of Chicago, 1891; emeritus member of the Illinois State Medical Society and member of the American Medical Association; also a pharmacist; on the staffs of the Grant and St. Elizabeth's hospitals and the City of Chicago Municipal Tuberculosis Sanitarium; died in Evanston (Ill.) Hospital June 10, aged 79, of primary bronchogenic carcinoma.

William Belitz, Cochrane, Wis.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1898; died April 17, aged 81, of carcinoma of the gastrointestinal tract.

Oscar Caraker, Olmsted, Ill.; St. Louis College of Physicians and Surgeons, 1908; member of the American Medical Association; served as president of the Pulaski County Medical Society; on the staff of St. Mary's Hospital in Cairo; died May 22, aged 64, of coronary thrombosis.

Joseph Wallace Chetwynd, East Liverpool, Ohio; Jefferson Medical College of Philadelphia, 1907; member of the American Medical Association; on the staff of the East Liverpool City Hospital; formerly on the staff of the Massillon (Ohio) State Hospital; died May 2, aged 63, of heart disease.

Harold Thompson Clapp, Cleveland; University of Wooster Medical Department, Cleveland, 1890; medical examiner and consultant for the Travelers Insurance Company; died in the Lakeside Hospital May 27, aged 76, of myocardial failure.

Milton Daily, Sioux City, Iowa; Minneapolis College of Physicians and Surgeons, medical department of Hamline University, 1895; member of the American Medical Association; formerly police surgeon; served as a member and president of the city school board; at one time medical examiner for the Cudahy Packing Company and the Stock Yards Company; on the staff of St. Vincent's Hospital, where he died May 8, aged 74, of embolism of the lung, fracture of the femur and diabetes mellitus.

Richard Ensign Dickson ✠ Holyoke, Mass.; Jefferson Medical College of Philadelphia, 1895; served as president of the Eastern Hampden Medical Association; on the staff of the Holyoke Hospital; died in the Wesson Memorial Hospital, Springfield, May 9, aged 78, of coronary thrombosis.

Ernest De Forest Hammond, Salt Lake City; John A. Creighton Medical College, Omaha, 1900; member of the American Medical Association; past president of the Salt Lake County Medical Society; president of the medical staff of the Holy Cross Hospital medical staff and served as chief surgeon for the Salt Lake and Utah Railroad Company; died in the Veterans Administration Facility May 1, aged 74, of coronary heart disease with decompensation.

Walter Childs Haviland ✠ Mansfield Depot, Conn.; Baltimore Medical College, 1904; specialist certified by the American Board of Psychiatry and Neurology, Inc.; member of the American Psychiatric Association and the New England Society of Psychiatry; in 1939 joined the staff of the Mansfield State Training School and Hospital, where he recently retired as senior physician; served on the staffs of the Connecticut State Hospital in Middletown, Conn., and the Worcester Insane Hospital, Worcester, Mass.; died May 14, aged 63, of heart disease.

Claude Turner Keyes, San Angelo, Texas; Memphis (Tenn.) Hospital Medical College, 1897; member of the American Medical Association; died in a local hospital May 8, aged 74, of carcinoma of the liver.

Jesse B. Lampton ✠ Sapulpa, Okla.; Hospital College of Medicine, Louisville, Ky., 1907; died March 28, aged 66, of coronary heart disease.

Daniel Isaiah Leatherman ✠ Greensburg, Pa.; College of Physicians and Surgeons, Baltimore, 1886; died March 31, aged 84, of angina pectoris.

Francis X. McCormick, Milwaukee; Marquette University School of Medicine, Milwaukee, 1925; member of the American Medical Association; police surgeon and an examining physician for the state athletic commission; died in St. Mary's Hospital May 18, aged 47, of cerebral hemorrhage and arterial hypertension.

Arthur Willis McDonough, Denver; the Hahnemann Medical College and Hospital, Chicago, 1910; member of the American Medical Association; served as president and secretary of the Colorado Homeopathic Society; died April 11, aged 66, of cerebral tumor.

Edward Lee McIntyre, Springfield, Ky.; Kentucky School of Medicine, Louisville, 1889; died April 15, aged 81, of bronchopneumonia.

Ralph J. Melman ✠ Philadelphia; Medico-Chirurgical College of Philadelphia, 1907; on the staffs of the Babies' and Northern Liberties hospitals; examining physician for the local draft board number 9; died April 10, aged 60, of coronary occlusion.

Francis A. Bernard Norton, Bakerstown, Pa.; University of Louisville (Ky.) Medical Department, 1902; died in the Schenley Nursing Home, Pittsburgh, March 14, aged 72, of arteriosclerotic heart disease and cerebral hemorrhage.

Gurdon Edgar Padget, Cuyler, N. Y.; Syracuse University College of Medicine, 1904; died May 4, aged 78, of coronary occlusion.

August Nob Pelusio, Paterson, N. J.; College of Physicians and Surgeons, Baltimore, 1913; died April 29, aged 64, of pulmonary edema and arteriosclerosis.

Everett Clifton Perkins, Dover, N. H.; Medical School of Maine, Portland, 1897; died April 3, aged 74, of cerebral hemorrhage.

Allan Ramsey, Cincinnati; Medical College of Ohio, Cincinnati, 1896; formerly assistant professor of medicine at the University of Cincinnati College of Medicine; served on the staff of the Children's Hospital; died in the Christ Hospital April 10, aged 75, of a fractured skull caused by a fall on a street car.

William Ford Richardson, Beech Creek, Ky.; Louisville Medical College, 1904; member of the American Medical Association; on the staff of the Muhlenberg Community Hospital in Greenville, where he died May 10, aged 74, of heart disease.

Silas M. Rohr, Santa Rosa, Calif.; Baltimore Medical College, 1889; died April 16, aged 84, of chronic myocardial degeneration and herpes zoster.

Reed Alonzo Sauter ✠ Schenectady, N. Y.; Albany Medical College, Albany, 1895; also a pharmacist; died March 7, aged 75, of coronary occlusion.

John Gottleib Schwarz, Gallipolis, Ohio; Ohio-Miami Medical College of the University of Cincinnati, 1912; served as superintendent of the Ohio Hospital for Epileptics, where he had been assistant superintendent and for many years on the staff; died in the Holzer Hospital April 19, aged 70, of chronic nephritis.

William Dodds Scott Jr., Baltimore; University of Maryland School of Medicine, Baltimore, 1904; served overseas during World War I; formerly affiliated with the U. S. Public Health Service; died in the Union Memorial Hospital April 16, aged 66, of congestive heart disease and hypertensive cardiovascular disease.

Beryl Whittier Scully, Rome, N. Y.; Cornell University Medical College, New York, 1933; member of the American Medical Association; interned at the Bellevue Hospital in New York; died April 28, aged 39, of a fractured skull received when his automobile hit a tree.

George F. Seiberling ✠ Allentown, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1893; on the staff of the Sacred Heart Hospital; member of the chamber of commerce; elected vice president of the board of directors of the Lehigh County Agricultural Society; died May 6, aged 75, of coronary thrombosis.

Arthur C. Sidler, Cudahy, Wis.; Milwaukee Medical College, 1897; formerly mayor of Cudahy; before Cudahy became a city he served as president of the village school board and health commissioner; died in Nashville, Tenn., March 31, aged 71, of arteriosclerotic heart disease.

Raymond Robinson Simmons ✠ Winston-Salem, N. C.; Medical College of Virginia, Richmond, 1917; on the courtesy staffs of the City Memorial and North Carolina Baptist hospitals; died May 5, aged 53, of aortic and myocardial insufficiency.

Henry Petway Spencer, Burns, Tenn.; University of Tennessee Medical Department, Nashville, 1907; died in White Bluff April 18, aged 67, of coronary thrombosis.

Richard Henry Stafford, Sumner, Iowa; Rush Medical College, Chicago, 1890; for many years city health officer; surgeon for the Chicago Great Western Railway; died April 8, aged 85, of cardiovascular disease and coronary thrombosis.

Nevin G. Stevenson, Sparta, Ill.; Chicago Homeopathic Medical College, 1895; member of the American Medical Association; superintendent and owner of the Sparta Community Hospital, where he died April 28, aged 74, of cerebral hemorrhage.

Charles C. Stockard, Lawrenceburg, Tenn. (licensed in Tennessee in 1909); member of the American Medical Association; past president of the Hardin-Lawrence-Lewis-Perry-Wayne Counties Medical Society; at one time company physician for the Napier Irons Works in Napier; commissioned a first lieutenant by Governor Prentice Cooper as examining physician for the National Guard; died May 6, aged 60, of pernicious anemia.

Robert Glenn Stone, Atlanta, Ga.; University of Georgia Medical Department, Augusta, 1906; member of the Medical Society of New Jersey, American Medical Association and the American Psychiatric Association; in 1919 joined the staff of the New Jersey State Hospital, Trenton, where he was for many years clinical director, and from 1930 until he retired on May 1, 1944 medical director; died April 27, aged 64, of cardiac decompensation and renal insufficiency.

Colletta Mayme Swaney, Detroit; Wayne University College of Medicine, Detroit, 1937; served an internship at the Eloise Hospital in Eloise, Mich., and a residency at the East Side General Hospital; found dead in her apartment April 18, aged 40, of heart disease, acute venous stasis, emphysema of the lungs and congestion of the kidneys.

John W. Swindell, Greenville, Texas; Memphis (Tenn.) Hospital Medical College, 1892; member of the American Medical Association; died April 20, aged 75.

Thomas F. Taylor, Dresden, Tenn.; University of Tennessee Medical Department, Nashville, 1898; member of the American Medical Association; died in Martin April 4, aged 75, of coronary thrombosis.

Guglielmo A. Tedesco, Union City, N. J.; Regia Università di Torino Facoltà di Medicina e Chirurgia, Italy, 1899; died in St. Mary's Hospital, Hoboken, April 28, aged 70, of coronary occlusion and hypertrophy of the prostate.

Marcus Thrane, Hood River, Ore.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1894; member of the American Medical Association; died April 10, aged 70, of coronary thrombosis.

Joel Adams Tilton Jr., Washington, D. C.; George Washington University School of Medicine, Washington, 1916; associated with the Veterans Administration; died April 28, aged 50, of coronary occlusion.

John Joseph Zaun Sr., Milwaukee; Rush Medical College, Chicago, 1901; on the staff of St. Mary's Hospital, where he died May 19, aged 65, of embolism.

PUBLIC HEALTH SERVICE

Leon Glassman ✠ Assistant Surgeon, U. S. Public Health Service Reserve, Philadelphia; Hahnemann Medical College and Hospital, Philadelphia, 1940; interned and served a residency in obstetrics and gynecology at the Hahnemann Hospital in Philadelphia; entered the public health service reserve as assistant surgeon and began active duty in October 1943; assigned to the outpatient department of the U. S. Marine Hospital, Baltimore; on May 5, 1944 transferred to the War Shipping Administration and assigned to the medical examination program; later in 1944 assigned to the U. S. Maritime Service Training Ship *American Engineer;* a short while later ordered to the Coast Guard, Captain of the Port, Baltimore; assigned to the District Coast Guard office, Sixth Naval District, Charleston, S. C., for the final tour of duty on Oct. 30, 1944, since which time he had been on sea duty with the Coast Guard as medical officer aboard a Coast Guard cutter; recommended for the Purple Heart; was buried in the Marine cemetery on Saipan; died May 4, aged 30, of injuries received when he slipped on the Jacob's ladder while helping load wounded marines aboard his ship.

Correspondence

METHYLENE BLUE TEST FOR BILIRUBIN IN THE URINE

To the Editor:—The editorial comment in THE JOURNAL, April 21, page 1059, discussed Myers' use of the methylene blue test for bilirubin in the urine. In Correspondence May 26, page 308, appeared a communication from Watson, Meads and Castle in which the value of the test as used by Myers was questioned because of its lack of specificity for bilirubin. For the past one and one-half years the methylene blue test has been under investigation in several laboratories engaged in the study of infectious hepatitis under the auspices of the Commission on Measles and Mumps, Army Epidemiological Board, Preventive Medicine Service, Office of the Surgeon General, U. S. Army. Our experience with a modified methylene blue test in several epidemics of infectious hepatitis and in hepatitis produced experimentally in human volunteers has indicated that the modified test is capable of providing valuable information concerning the presence of bilirubin in the urine. A brief discussion of the technic and interpretation of the methylene blue test, as used in our studies, may aid in reconciling the favorable experience of Myers with the unfavorable opinion expressed by Watson, Meads and Castle. The test was performed by Myers and by Watson and her associates by adding 2 drops of methylene blue to 10 cc. of urine. The occurrence of a green color apparently has been interpreted as a positive test for bilirubin in the urine. Unfortunately, experience has shown that the addition of 2 drops of methylene blue to certain urines which do not contain bilirubin is followed by the development of a green color. Our experience indicates that this objection to the test can be eliminated by modifying the technic and interpretation.

The cause of the green color produced by the addition of methylene blue to certain urine specimens has been subject to controversy since the beginning of the century. Experiments such as those described by Watson and her associates indicate that the blending of the yellow pigments of urine, regardless of their nature, with methylene blue (or other blue solutions) produces a green color. This is the explanation for the green color occurring after the addition of 1 to 4 drops of methylene blue to certain urines that do not contain bilirubin. However, tests of a large number of supposedly normal and pathologic urines have indicated that no commonly occurring urine pigments other than bilirubin produce sufficient yellow color to require more than 4 drops of methylene blue to extinguish the green color resulting from the blending of blue and yellow.

For this reason we have performed and interpreted the test as follows: An aqueous solution of methylene blue (0.2 per cent based on actual dye content) is added drop by drop to 5 cc. of urine and the total number of drops required to impart a blue color to the urine-methylene blue mixture is noted. If more than 8 drops are required a smaller measured amount of urine is diluted to 5 cc. and the test repeated in order that a clearer end point may be obtained. If diluted, the number of drops is multiplied by the dilution factor. The reading (in drops) is taken as one less than the number needed to change the color from green to blue. A reading greater than 4 drops has been regarded as a positive test for bilirubin in the urine. Although the sensitivity of the test was diminished by the use of this criterion, its specificity was increased greatly, as indicated by the infrequent occurrence of falsely positive tests. Readings of 2 to 4 drops inclusive have been regarded as suggestive and as an indication for additional studies. As already stated, our investigations of this modified methylene blue test have been confined almost entirely to the study of urines from patients with infectious hepatitis. In this condition the modified test has yielded information of considerable value both in respect to early diagnosis and as a simple means of following the course of the disease. Furthermore, positive tests have been obtained with the urines from many hepatitis patients before the appearance of overt jaundice. An additional contribution of the test has been the roughly quantitative information it provides concerning changes in the excretion of bilirubin in the urine.

The methylene blue test, in our experience, has been inferior in sensitivity and specificity to the Harrison and diazo "spot" tests for bilirubin in the urine. On the other hand, when positive, it provides better quantitative evidence concerning the output of urine bilirubin than is afforded by the "spot" tests and it can be performed under conditions which do not permit the use of the latter. For these reasons it is our opinion that the modified methylene blue test, properly used and interpreted, will prove to be a valuable procedure.

Conclusive evidence has been obtained (by J. G. Reinhold and others) that a chemical reaction occurs between methylene blue and bilirubin. Spectrophotometric studies have revealed alterations in the absorption spectrums of methylene blue and bilirubin when the two were combined in aqueous solution. Furthermore, a green precipitate was obtained by the addition of methylene blue to bilirubin in weakly alkaline solutions. A similar precipitate appeared on standing after adding methylene blue to neutral or weakly alkaline urines containing bilirubin (obtained from patients with hepatitis). However, it is believed that this chemical reaction is less important than the blending of blue and yellow colors in explaining the green color constituting the positive methylene blue test.

SYDNEY S. GELLIS, Captain, M. C., A. U. S.
JOHN R. NEEFE, Captain, M. C., A. U. S.
JOHN G. REINHOLD, PH.D.
JOSEPH STOKES JR., M.D.
Maloney Clinic, Hospital of the University of Pennsylvania, Philadelphia 4.

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

NATIONAL BOARD OF MEDICAL EXAMINERS EXAMINING BOARDS IN SPECIALTIES

Examinations of the National Board of Medical Examiners and Examining Boards in Specialties were published in THE JOURNAL, July 7, page 762.

BOARDS OF MEDICAL EXAMINERS

ALASKA: Juneau, September. Sec., Dr. W. M. Whitehead, Box 561, Juneau.

CALIFORNIA: *Oral.* Los Angeles, Aug. 11. Sec., Dr. Frederick N. Scatena, 1020 N St., Sacramento 14.

CONNECTICUT: * *Endorsement.* New Haven, July 24. Sec. to the Board, Dr. Creighton Barker, 258 Church St., New Haven.

DELAWARE: *Reciprocity.* Dover, July 17. Sec., Medical Council of Delaware, Dr. J. S. McDaniel, 229 S. State St., Dover.

INDIANA: Indianapolis, Aug. 28-30. Sec., Board of Medical Registration & Examination, Dr. W. C. Moore, 301 State House, Indianapolis 4.

MONTANA: Helena, Oct. 1-3. Sec., Dr. O. G. Klein, First Nat'l. Bank Bldg., Helena.

NEVADA: *Reciprocity.* Carson City, Aug. 6. Sec., Dr. G. H. Ross, 215 N. Carson St., Carson City.

NEW MEXICO: * Santa Fe, Oct. 8-9. Sec., Dr. LeGrand Ward, 141 Palace Ave., Santa Fe.

OHIO: *Endorsement.* Columbus, July. Sec. Dr. H. M. Platter, 21 W. Broad St., Columbus.

OREGON: * Portland, July 25-27. Exec. Sec., Miss L. M. Conlee, 608 Failing Bldg., Portland 4.

SOUTH DAKOTA: * Pierre, July 17-18. Sec., Medical Licensure, State Board of Health, Dr. Gilbert Cottam, State Capitol, Pierre.

TEXAS: Houston, July 17-19. Sec., Dr. T. J. Crowe, 918-20 Texas Bank Bldg., Dallas 2.

WASHINGTON: * Seattle, July 16-18. Sec., Department of Licenses, Miss Nell Adams, Olympia.

* Basic Science Certificate required.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

MICHIGAN: Ann Arbor and Detroit, Oct. 12-13. Sec., Miss Eloise LeBeau, 101 N. Walnut St., Lansing.

NEBRASKA: Omaha, Oct. 2-3. Dir., Bureau of Examining Boards, Mr. Oscar F. Humble, 1009 State Capitol Bldg., Lincoln 9.

RHODE ISLAND: Providence, Aug. 15. Chief, Division of Examiners, Mr. Thomas Casey, 366 State Office Bldg., Providence.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1935 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Heart Journal, St. Louis

29:419-554 (April) 1945

Management of Myxedematous Patient with Symptoms of Cardiovascular Disease. T. H. McGavack, K. Lange and D. Schwimmer.—p. 421.
Electrocardiographic Study of Deformity of Chest. A. R. Adorno and P. D. White.—p. 440.
Auricular Premature Systole: I. Aberration of Ventricular Complex in Electrocardiogram. K. Berliner and L. P. Lewithin.—p. 449.
Wolff-Parkinson-White Syndrome with Unusual Features. M. H. Stein. —p. 479.
Comparison of Therapeutic Effectiveness of Serum and Sodium Chloride in Scald Shock. O. Hechter, H. C. Bergman and M. Prinzmetal. —p. 484.
Role of Renal Pressor System in Burn Shock. O. Hechter, H. C. Bergman and M. Prinzmetal.—p. 493.
Further Studies on Liver Principle Which Is Effective Against Burn Shock. O Hechter, H. C. Bergman, L. Sapirstein, R. Fisk, G. Feigen and M. Prinzmetal.—p. 499.
Ineffectiveness of Adrenocortical Hormones, Thiamine, Ascorbic Acid, Nupercaine and Post-Traumatic Serum in Shock Due to Scalding Burns. H. C. Bergman, D. D. Rosenfeld, O. Hechter and M. Prinzmetal.—p. 506.
Effect of Short Term Nutritional Stress on Resistance to Scald Shock. H. C. Bergman, O. Hechter and M. Prinzmetal.—p. 513.
Urologic Disease as Cause of Hypertension. M. M. Rath and H. I. Russek.—p. 516.
Morphologic Study of Cardiac Conduction System: Part IV. Anatomy of Upper Part of Ventricular Septum in Man. D. J. Glomset and R. F. Birge.—p. 526.

American Journal of Clinical Pathology, Baltimore

15:87-122 (March) 1945

*Tumors of Thymus in Myasthenia Gravis. N. A. Murray and J. R. McDonald.—p. 87.
*Rh Antibodies. I. Davidsohn.—p. 95.
Rh-Blood Types and Some of Their Applications. A. S. Wiener. —p. 106.

Tumors of Thymus in Myasthenia Gravis.—Murray and McDonald studied thymus glands removed from 10 fetuses and from 100 persons from the ages of 4 months to 86 years. They also studied thymomas associated with myasthenia gravis in 13 cases and 2 thymic tumors removed surgically from patients with myasthenia gravis. Several observations made by them suggested that these tumors are thymomas. Most primary tumors of the thymus associated with myasthenia gravis are of a single type. They are made up of lymphocytes and larger pale cells that have faintly acidophilic cytoplasm in varying proportions and indefinite cell boundaries. These tumors contain numerous small blood vessels and occasional Hassall's corpuscles. A "lining up" or palisading of the pale cells along connective tissue trabeculae and pseudorosette formation around blood vessels appear to be distinguishing features. If metastasis and direct extension are sufficient criteria for the diagnosis of malignancy, then these tumors are malignant. It is believed that "thymoma" is an adequate name for these tumors. Those which will metastasize cannot be distinguished from those which will not metastasize. The absence or presence of secondary germ centers (lymph follicles) does not point either to or away from malignancy. The absence of differentiation between cortex and medulla is not a reliable criterion for the diagnosis of malignancy. The incidence of myasthenia gravis among patients with thymoma is nearly 100 per cent. Eaton has stated that the incidence of thymomas among patients with myasthenia gravis is 14 per cent. According to Bell the incidence at necropsy of thymic dysplasia among patients who have died of myasthenia gravis is about 50 per cent.

Rh Antibodies.—Davidsohn says that the titer of anti-Rh agglutinins in the blood of mothers of children with erythroblastosis is highest from about eight to twenty days following delivery, and this is the best time for testing for anti-Rh agglutinins and for obtaining potent anti-Rh serum. The prozone phenomenon (failure of antigen-antibody reaction in undiluted serum, but manifest reaction in higher dilutions) is not infrequent in anti-Rh serum. Therefore, when testing for anti-Rh agglutinins, serum dilutions up to 1:20 should be examined. The presence of anti-Rh agglutinins during pregnancy does not necessarily spell erythroblastosis in the baby about to be born, particularly if the antibodies may be ascribed to a preceding pregnancy. Erythroblastosis may be due to Rh incompatibility even in case of Rh-positive mothers. Among factors of possible prognostic significance with regard to future pregnancies, the following two considerations may have to be included: (*a*) the homozygocity or heterozygocity of the husband if determinable; (*b*) the persistence of anti-Rh agglutinins following birth of a child with erythroblastosis.

American Journal of Physiology, Baltimore

143:463-634 (April) 1945. **Partial Index**

Dynamics of Isolated Heart and Heart-Lung Preparations of Dog. L. N. Katz, W. Wise and K. Jochim.—p. 463.
Proximodistal Fluid Convection in Endoneurial Spaces of Peripheral Nerves, Demonstrated by Colored and Radioactive (Isotope) Tracers. P. Weiss, Hsi Wang, A. C. Taylor and M. V. Edds Jr.—p. 521.
Efficiency of Glare Reduction by Eyelids. E. Simonson, S. S. Blaukenstein and E. J. Carey.—p. 541.
Effect of Adrenocorticotropic Hormone on Survival of Normal Rats During Anoxia. Choh Hao Li and V. V. Herring.—p. 548.
Use of Cholinesterase in Shock. R. J. Schachter.—p. 552.
Effect of Adrenalectomy on Potassium of Stimulated Muscle. J. R. Jordan.—p. 558.
Contents of Stomach, Small Intestine, Cecum and Colon of Normal and Fasting Rabbits. E. B. Carmichael, J. T. Strickland and R. L. Driver.—p. 562.
Dehydrating Effect of Continuously Administered Water. A. V. Wolf. —p. 567.
Effect of Hemorrhage on Lactate/Pyruvate Ratio and Arterial-Venous Differences in Glucose and Lactate. Clarissa H. Beatty.—p. 579.
Rate of Carbon Monoxide Uptake by Normal Men. W. H. Forbes, F. Sargent and F. J. W. Roughton.—p. 594.
Average Time Spent by Blood in Human Lung Capillary and Its Relation to Rates of CO Uptake and Elimination in Man. F. J. W. Roughton.—p. 621.

American Journal of Surgery, New York

130:139-278 (May) 1945

Treatment of Abdominal Injuries: Review of 88 Personal Cases. J. L. Dixon, G. Martin and A. Ochsner.—p. 143.
*Air Embolism: Fatal Air Embolism Due to Powder Insufflators Used in Gynecologic Treatments. H. S. Martland.—p. 164.
Refrigeration in General Surgery of Limbs. F. M. Allen.—p. 170.
*Positive Pressure Respiration in Treatment of Acute Pulmonary Edema. F. P. Ansbro.—p. 185.
Skin Grafting by General Surgeon. J. C. Urkov.—p. 195.
New Technic for Reconstruction of Oviducts. D. Polowe.—p. 208.
Nonsplinting Treatment of Elbow Joint Injuries: Report of Its Use in 20 Cases. T. A. Boutrous, A. Blain and W. A. Chipman.—p. 212.
Acute Cholecystitis: Comparative Study of Mortality Rate After Immediate and Delayed Operations. W. J. McGuigan.—p. 219.
Cellophane in Bone and Joint Surgery. G. H. Harley and L. W. Breck. —p. 229.
Sulfathiazole-Cod Liver Oil Ointment in Postoperative Care of Septic Hand. D. Brezin.—p. 232.

Fatal Air Embolism Due to Power Insufflators.—Martland investigated two deaths occurring after vaginal insufflation of medicinal powders for the relief of pruritus vulvae. In the first case a virginal and cribriform hymen played an important role in the causation of the air embolism. The doctor, believing he was spraying powder over the external genitals, must have unknowingly held the glass tip of the insufflator directly over the largest opening in the hymen and have blown powder and air into the vagina. The air entrapped in the vagina was forced into the uterine cavity. The exact point of entry of air into the venous circulation cannot be demonstrated. The fact that the patient had just passed a menstrual period favors engorgement and distention of the uterine veins. The second woman was six months pregnant. In this case the metal end of the insufflator must have rested against the soft cervix of the pregnant uterus and considerable powder and large amounts of air were blown directly into the uterine cavity. The main purpose of the insufflators is to dilate and smooth out the folds

in the vagina so that the powder may be sprayed on the mucosa. It is obvious that the sudden blowing up of the vagina with air under excessive pressure is not without danger. The engorgement of the endometrium around the menstrual period, open veins after uterine curettage and the soft cervix of a pregnant uterus all might favor air embolism during such insufflations. It is reasonable to assume that few of these catastrophes are likely to be reported and that perhaps some such deaths have been attributed to heart disease or some other condition and never verified by necropsy.

Positive Pressure Respiration for Pulmonary Edema.—Ansbro reports 2 cases of acute pulmonary edema in which positive pressure respiration with oxygen was followed by a prompt clearing of the condition and recovery. The first patient took an overdose of sedative medication the night and morning before operation. Respiratory depression following the operative procedure was considered the initial cause of the widespread pulmonary edema that ensued. Inhalation of oxygen by catheter, mask and tent failed to relieve either the cyanosis or the edema. The application of positive pressure by the anesthesia mask resulted in a swift clearing of edema and cyanosis. The pulmonary edema in the second patient probably resulted from the primary tracheal obstruction (which necessitated the tracheotomy) and was aggravated by the ensuing ball valve action of the wet gauze at the tube opening, which resulted in an increased negative intrapulmonary pressure. The removal of the ball valve produced some improvement; the patient was literally "drowning in her own secretions" until positive pressure respiration dammed back the fluid. It is recommended that positive pressure respiration be adopted in combating what is frequently regarded as a terminal event.

American Review of Soviet Medicine, New York

22:291-384 (April) 1945

Treatment of Spinal Column and Spinal Cord Wounds. N. I. Propper-Grashchenkov.—p. 292.
Agonal States and Clinical Death: Problems in Revival of Organisms. V. A. Negovski.—p. 303.
Radiotherapy and Intracranial Pressure. Maria B. Tsuker.—p. 316.
Refrigeration Anesthesia in Surgery of Extremities. S. V. Lobachev. —p. 323.
Susceptibility of Macacus Rhesus to Virus of Tick Borne Encephalitis. L. A. Silber and A. K. Shubladze.—p. 332.
Louping Ill in U. S. S. R. L. A. Silber and A. K. Shubladze.—p. 339.
Cytology and Karyology of Colon-Typhoid Group. M. A. Peshkov. —p. 342.
Carbonic Acid in Formation of Amino Acids by Surviving Animal Tissues. M. G. Kritzmann.—p. 349.
Symptom of "Electrical Discharge" in Brain Injuries. A. V. Triumfov. —p. 350.
Stimulating Visual Function. S. V. Kravkov.—p. 353.
Therapeutic and Prophylactic Use of Grip Antivirus. D. M. Rossiski. —p. 356.

Archives of Internal Medicine, Chicago

75:215-278 (April) 1945

Arachnodactyly (Spider Fingers). H. Gray.—p. 215.
Primary Atypical Pneumonia of Unknown Cause. R. C. Schmitz.—p. 222.
*Effects of Cold Air on Air Passages and Lungs: Experimental Investigation. A. R. Moritz and J. R. Weisiger.—p. 233.
*Fatal Poisoning from Potassium Thiocyanate Used in Treatment of Hypertension: Report of Case and Review of Literature. A. del Solar, G. Dussaillant G., M. Brodsky B. and G. Rodriguez C.—p. 241.
Venesection for Plethoric Patient. L. E. Hines and D. L. Kessler. —p. 248.

Effects of Cold on Air Passages.—Moritz and Weisiger caused dogs to breathe extremely cold air for periods ranging between twenty and one hundred and thirty-three minutes. The rate at which air was warmed within the body was measured by means of appropriately placed thermocouples. The air was delivered to the larynx at temperatures which ranged between — 50 and — 28 C., and in no instance were temperature recordings lower than + 18 C. observed at the bifurcation of the trachea. The explanation of the rapid warming of inhaled cold air and of the occurrence of relatively mild and localized injury following the inhalation of cold air lies in the fact that dry air has an extremely low heat capacity and that the number of calories required to produce a great rise in the temperature of dry air can be provided by the heat derived from the cooling of a small amount of tissue by a few degrees. Although the intermittent exposure to cold air that occurs during normal respiration does not cause significant injury to the pharynx or larynx, a continuous exposure of these structures to cold may result in the development of a rapidly obstructive edema. Experiments on dogs warrant the inference (1) that it is unlikely that significant injury to the air passages of man would result from the breathing of air at any degree of coldness likely to be encountered in nonexperimental conditions as long as it was inhaled through the nose or between partially closed lips and (2) even though extremely cold air was inhaled rapidly through a widely opened mouth, it would be warmed to a point well above freezing by the time it reached the bronchi.

Fatal Poisoning with Potassium Thiocyanate.—Del Solar and his associates gave potassium thiocyanate to 73 patients with hypertension. In the fatal case which they report a distinct fault in dosage on the part of the patient was responsible for the intoxication. The case emphasizes the danger of prescribing the drug in easily inaccurately measured forms, like the solution for drop administration. The thiocyanate concentration of the blood at the onset of toxic symptoms was only 7 mg. per hundred cubic centimeters. The concentrations of the drug in the tissues are the highest ones thus far reported in similar instances. A prominent feature of the postmortem examination was the finding of an acute necrotic nephrosis that had produced no symptoms or signs during life.

Archives of Ophthalmology, Chicago

33:265-340 (April) 1945

Choice of Operation for Primary Glaucoma Combined with Cataract. J. S. Guyton.—p. 265.
Resection of Levator Palpebrae Muscle for Ptosis, with Anatomic Studies. R. N. Berke.—p. 269.
Uveitis, with Poliosis, Vitiligo, Alopecia and Dysacousia (Vogt-Koyanagi Syndrome). E. Rosen.—p. 281.
Meridional Aniseikonia at Oblique Axes. H. M. Burian and K. N. Ogle.—p. 293.
Heterochromia Sympathica. P. H. Boshoff and J. J. Theron.—p. 311.
Plastic Corneal Bath for Application of Penicillin. H. A. G. Duncan. —p. 313.

Canadian Medical Association Journal, Montreal

52:327-444 (April) 1945

Penicillin Agar Pastilles. P. Greey and I. B. Macdonald.—p. 327.
Psychoneurotics Discharged from Canadian Army. J. D. Griffin, W. D. Ross, G. H. Josie and M. F. Henderson.—p. 330.
Penicillin Therapy in Skin Infections. N. M. Wrong.—p. 341.
Acute Fluoride Poisoning. I. M. Rabinowitch.—p. 345.
Mental Illness and Principles of Medicine. J. G. Dewan and T. Owen. —p. 349.
Further Observations on Experimental Bone Formation with Special Reference to Bone-Forming Properties of Epithelial Lining of Trigone in Dog. A. C. Abbott and E. Stephenson.—p. 358.
Thiouracil. E. M. Boyd and W. F. Connell.—p. 362.
*Agranulocytic Angina Effectively Treated with Intravenous Pyridoxine (Vitamin B_6). M. M. Cantor and J. W. Scott.—p. 368.
Critical Survey of Two Diagnostic Pregnancy Tests (Colostrum Intracutaneous Test and Histidine Test). J. F. Davey and D. E. Daley. —p. 371.
Rupture of Uterus: An Analysis of 53 Cases. E. Delfs and N. J. Eastman.—p. 376.
Acute Inversion of Uterus. T. E. Nugent and M. H. MacKinnon. —p. 381.
Intravenous Use of Novocain as Substitute for Morphine in Postoperative Care. J. A. McLachlin.—p. 383.
Ancillary Services in Industrial Hygiene. N. L. Burnett.—p. 386.
Curare: New Tool for Anesthetist. H. R. Griffith.—p. 391.
New Rocker Type of Cast-Walker: Preliminary Report. A. M. Vineberg and D. R. Murphy.—p. 394.
Hemorrhagic Disease of Newborn. P. E. Williams.—p. 397.
Vasomotor Rhinitis. W. P. E. Paterson.—p. 400.

Pyridoxine (Vitamin B_6) in Granulocytopenia.—Cantor and Scott point out that the list of drugs likely to cause granulocytopenia has been lengthened year by year and now includes a number of coal tar derivatives, the barbiturates, the sulfonamides, gold salts and thiouracil. They report 3 cases of granulocytopenia successfully treated with pyridoxine (vitamin B_6). The pyridoxine was given daily by intravenous injection in doses of 125 or 200 mg. The material used was a 10 per cent solution of pyridoxine hydrochloride in isotonic solution of sodium chloride. This was put up in 10 cc. rubber capped vials and autoclaved for thirty minutes at 15 pounds pressure. The rapid and uniform response observed in these cases leads the authors to suggest that pyridoxine is the factor in liver and liver extracts responsible for the granulocytopoietic effect noted when liver is administered in granulocytopenia. Pyridoxine

produces granulocytopoiesis by an effect of the myelocytic elements of the bone marrow. It seems probable that pyridoxine is the factor involved in the maturation and emigration of the polymorphonuclear leukocyte.

Cancer Research, Baltimore

5:257-320 (May) 1945

Sarcomatous Transformation of Stroma of Mammary Carcinomas That Stimulated Fibroblastic Growth in Vitro. R. J. Ludford and Hilda Barlow.—p. 257.
9,10-Dimethyl-1,2-Benzanthracene as Highly Potent Carcinogen for Rabbit's Skin. I. Berenblum.—p. 265.
Heterologous Transplantation of Mouse and Rat Tumors. H. S. N. Greene and E. D. Murphy.—p. 269.
Thymonucleic Acid in Tumors. R. E. Stowell.—p. 283.
Relative Thymonucleic Acid Content of Human Normal Epidermis, Hyperplastic Epidermis and Epidermoid Carcinomas. R. E. Stowell and Zola K. Cooper.—p. 295.
Respiratory Behavior of Bacteria-Free Crown Gall Tissues. P. R. White.—p. 302.

Endocrinology, Springfield, Ill.

36:245-290 (April) 1945

Oxidation Reduction Potential of Thyroid Follicle in Normal and Experimental Conditions. E. De Robertis and J. Moura Gonçalves.—p. 245.
Study of Effect of Prolactin on Broodiness and on Cock Testes. A. V. Nalbandov, M. Hochhauser and Marie Dugas.—p. 251.
Metabolism of Rats After Thyroidectomy or During Thiouracil Treatment, and Effect of Thyroid Feeding. A. E. Meyer and G. V. Ransom.—p. 259.
Variations in Water Content of Rat's Uterus During Continuous Estrogenic Treatment. W. R. Carroll.—p. 266.
Response to Thyroxine After Subtotal Hepatectomy. P. E. Kellaway, H. E. Hoff and C. P. Leblond.—p. 272.

Epidemiological Information Bull., Washington, D. C.

1:205-246 (March 15) 1945

Evolution of Tuberculosis in France During War.—p. 207.
Memorandum on Chief Changes Made by International Sanitary Conventions, 1944. N. M. Goodman.—p. 219.
Current Reports on Prevalence of Certain Diseases: A. Data on Plague, Cholera, Yellow Fever, Smallpox and Typhus Received During the Period March 1 to March 15, 1945.—p. 228.
Id.: B. Data on Other Diseases: Cerebrospinal Meningitis Cases, May-December 1944.—p. 238.
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1:247-288 (March 31) 1945

International Sanitary Convention of June 1926 Modified by International Sanitary Convention of 1944: Preliminary Disposition.—p. 247.

Gastroenterology, Baltimore

4:205-288 (March) 1945

*Atabrine Dihydrochloride (Quinacrine Hydrochloride): Some Observations on Its Toxicity and on Its Use in Treatment of Malaria, with Particular Reference to Its Effects on the Liver. H. R. Butt, J. E. Hall, C. H. Watkins and R. W. Cragg.—p. 205.
Digestive Diseases in Station Hospital Overseas: Observations Over a Two Year Period. B. D. Rosenak and L. M. Foltz.—p. 213.
Interdigestive Discharge of Duodenal Content: I. Rate of Discharge. Four Rhythms. W. V. Berger and E. Oppenheim.—p. 228.
Osmotic Pressure of Fasting Jejunal Secretions in Man. L. C. McGee and A. B. Hastings.—p. 243.
Pepsin Secretion in Response to Caffeine. M. I. Grossman, J. A. Roth and A. C. Ivy.—p. 251.
Some Observations of Changes in Renal Water Output of Albino Rat Under Influence of High Fat Diet. H. Shay, R. Kolm and S. S. Fels.—p. 257.

Effect on Liver of Atabrine Dihydrochloride (Quinacrine Hydrochloride).—Butt and his associates administered to 50 white men between the ages of 19 and 35 years 4.5 Gm. of atabrine over a ten day period. All of these patients had had malaria with multiple relapses. Prior to the administration of atabrine and again at the completion of the ten day course of atabrine therapy the following laboratory procedures were carried out: (1) sulfobromophthalein test for hepatic function; (2) prothrombin time (Quick's method); (3) serum bilirubin; (4) van den Bergh reaction; (5) erythrocyte, leukocyte and differential count; hemoglobin estimation and a special blood smear for macrocytosis; (6) thick blood smear for malaria parasites. There was little evidence that atabrine exerted much, if any, hepatoxic action. The toxic reactions reported in this and other studies have been few and of only moderate severity. To hesitate to use atabrine because of the possible untoward reactions does not seem justified.

Journal of Experimental Medicine, New York

81:405-538 (May) 1945

Hemoglobin and Plasma Protein: Their Relation to Internal Body Protein Metabolism. L. L. Miller, Frieda S. Robscheit-Robbins and G. H. Whipple.—p. 405.
Synthesis, Storage and Excretion of Creatine, Creatinine and Glycocyamine in Progressive Muscular Dystrophy and Effects of Certain Hormones on These Processes. C. L. Hoagland, Helena Gilder and R. E. Shank.—p. 423.
Tolerance to Amino Acid Mixtures and Casein Digests Given Intravenously: Glutamic Acid Responsible for Reactions. S. C. Madden, R. R. Woods, F. W. Shull, J. H. Remington and G. H. Whipple.—p. 439.
Comparison of Human and Guinea Pig Complements and Their Component Fractions. O. G. Bier, Graciela Leyton, M. M. Mayer and M. Heidelberger.—p. 449.
Regenerative Cycle of Motoneurons, with Special Reference to Phosphatase Activity. D. Bodian and R. C. Mellors.—p. 469.
Cytochrome Oxidase in Normal and Regenerating Neurons. H. A. Howe and R. C. Mellors.—p. 489.
Reversible Inactivation of Substance Inducing Transformation of Pneumococcal Types. M. McCarty.—p. 501.
Plasma Protein Metabolism—Electrophoretic Studies: Restoration of Circulating Proteins Following Acute Depletion of Plasmapheresis. L. J. Zeldis and E. L. Alling.—p. 515.

Journal of Immunology, Baltimore

50:191-254 (April) 1945

Antigen-Antibody Reactions in Salmonella Group: Introduction—Complement Fixation—Precipitation—Agglutinin Inhibition—Antigenicity—General Conclusions. E. Seligmann.—p. 191.
Use of Refined Serum Albumin as Nutrient for T. Pallidum. P. A. Little and Y. Subbarow.—p. 213.
Serologic Relationship Amongst Salmonella and Other Enterobacteriaceae. I. Saphra and M. Wassermann.—p. 221.
Role of Pathogenicity Enhancing Substance in Mice Infected with Shigella Dysenteriae (Shiga) and Other Enterobacteriaceae. L. Olitzki and P. K. Koch.—p. 229.
Studies on Listeria Monocytogenes: II. Effect of Heat and Alcohol on Stable Somatic Antigens. Mary L. Robbins and A. M. Griffin.—p. 237.
Id.: III. Antibody Response to Individual Components of Antigen Mosaic During Immunization. Mary L. Robbins and A. M. Griffin.—p. 247.

Journal of the Mount Sinai Hospital, New York

11:317-374 (March-April) 1945

Recent Advances in Histochemistry. G. Gomori.—p. 317.
*Wound Infections in Diabetic Surgical Patients: Analysis of 34 Cases. R. W. Watson.—p. 327.
Glioma of Optic Nerve. H. M. Katzin.—p. 332.
Acute Suppurative Labyrinthitis and Bacterial Meningitis, Labyrinthectomy, Recovery: Report of Case. J. G. Druss.—p. 336.
Life's Later Years: Studies in Medical History of Old Age; Medicine of Islam. F. D. Zeman.—p. 339.
Massive Pulmonary Embolism: V. Based in Part on Study of 88 Fatal Cases. H. Neuhof and S. H. Klein.—p. 345.
Essays on Biology of Disease: Obesity. E. Moschcowitz.—p. 357.

Wound Infections in Diabetic Surgical Patients.—Watson presents observations on 34 patients with a history of preceding diabetes mellitus who were operated on for some pathologic condition having no direct relation to their glycosuria. The diabetes was well controlled in these patients. With the exception of two thyroidectomies and one hernioplasty, every patient was subjected to laparotomy. Fifteen of the wounds healed by primary union; 19 of the wounds became infected. A comparative study of operative wounds of an equal number of nondiabetic surgical patients was made for control purposes. Wound infections developed in 3 of the 34 cases selected. Postoperative wound infections were almost six times more frequent in the diabetic group. This susceptibility is in large part due to the greatly lowered tissue resistance inherent in the diabetic patient.

Journal of National Cancer Inst., Washington, D. C.

5:311-382 (April) 1945

Gastric Physiology in Relation to Gastric Cancer. A. C. Ivy.—p. 313.
Genetic Analysis of Induction of Tumors by Methylcholanthrene: IX. Induced and Spontaneous Adenocarcinomas of Stomach in Mice. L. C. Strong.—p. 339.
Superficial Spreading Type of Carcinoma of Stomach. A. P. Stout.—p. 363.
Radical Surgery for Gastric Cancer. A. Brunschwig.—p. 365.
Physiology of Mucus Secretion. F. Hollander.—p. 367.
Excretion of Sulfa Drugs by Stomachs of Normal Persons and Patients with Gastritis, Peptic Ulcer and Gastric Cancer. L. Schiff.—p. 369.
Disturbances of Sugar Metabolism in Gastric Cancer. H. O. Singher.—p. 371.
Multiple Cancers of Human Gastrointestinal Tract. S. Warren.—p. 375.
Observations of Chronic Gastritis and Cancer. W. A. Meissner.—p. 377.

Journal of Nervous and Mental Diseases, New York

101:401-514 (May) 1945

War Psychiatry and Its Influence on Postwar Psychiatry and on Civilization. E. A. Strecker.—p. 401.
Psychiatry Before World War II. S. W. Hamilton.—p. 416.
Present and Future Effects of War Neuroses. C. C. Burlingame.—p. 429.
Civilian Advances and Investigations in Neurosurgery During the War. C. Pilcher.—p. 434.
War Neuroses or Battle Fatigue? R. R. Grinker.—p. 442.
War and Its Psychiatric Problems. H. P. Rome.—p. 445.
Injuries to Central Nervous System. W. M. Craig.—p. 451.
*Injuries to Peripheral Nervous System: War Wounds and Organization for Their Care. H. C. Naffziger.—p. 453.
Two Important Postwar Problems in Neurologic Surgery. E. Sachs.—p. 460.
Compensation Laws and the Veterans Administration. D. J. Margolis.—p. 462.

Injuries to Peripheral Nervous System in War.—Naffziger thinks that under the best conditions the results of surgery of the peripheral nerves leave much to be desired. The functional result depends on the integrity of the entire neuromuscular mechanism. Much more is involved than merely regeneration of a nerve. Muscles destroyed or fibrosed cannot act even though nerve supply returns. Injuries to major vessels with ischemia, when associated with palsies of the nerves, constitute one of the most severe conditions. We have little to offer the victims of traction injuries in which, through stretching, the damage to fibers is spread over great lengths of the nerve. The affected nerve, though remaining in gross continuity, contains widely scattered areas of rupture and degeneration. Suture of nerves is time consuming and is not practicable in the rush of urgent war surgery. It is a sound surgical principle to allow considerable time after complete healing of a wound before repair of a nerve is attempted. As regards organization of our medicomilitary establishment, we have profited neither from our experiences in the last war nor from the example of our British allies. British military forces are cared for by 3.5 medical men per thousand, as compared to about 6.0 used by our army. More highly specialized care is being given by the English than is available to our forces, in spite of the fact that Great Britain has proportionately fewer medical men. They have accomplished this without waste of medical manpower by utilizing existing facilities. Of the five British peripheral nerve centers, four are associated with or are near medical schools. They are staffed principally by civilians. In addition to the surgeon, neurologists, neurophysiologists, neuropathologists, orthopedists and special technical help from the medical schools participate and form a team. Among the directing surgeons are some who had a vast experience in this type of surgery in the last war. In the United States, three years of war have resulted in the designation of certain general hospitals for peripheral nerve cases. The specialized staffs consist of young neurologic surgeons, mostly well trained in the fundamentals of the specialty but without previous opportunity to familiarize themselves with the diagnosis and therapy of injuries to peripheral nerves. If the hospitals were located near medical schools, the staffs of these schools would supplement the study and care of the patients and, in addition, the military hospitals would serve as training centers for the specialists of tomorrow. Such opportunities cannot be duplicated and should not be lost.

Missouri State Medical Assn. Journal, St. Louis

42:257-316 (May) 1945

*Penicillin in Treatment of Gonorrhea. D. R. Seabaugh.—p. 273.
Diagnosis of Thromboangiitis Obliterans and Peripheral Arteriosclerosis. P. S. Lowenstein.—p. 277.

Penicillin in Treatment of Gonorrhea.—Seabaugh found that 100,000 units of penicillin is productive of cures in 74.3 per cent of cases of gonorrhea. This percentage of cures may be increased to 95 by the administration of additional penicillin. Five per cent of the cases treated did not respond to 400,000 units of the drug. The effectiveness of penicillin is not dependent on the age or chronicity of the lesion. After a clinical and bacteriologic cure, 6.1 per cent of the total cases treated will undergo a relapse within the first ten days. Another 11.9 per cent of the total cases treated will show a primary reduction of the discharge to only a morning tear with negative prostatic cultures and also undergo a relapse back to an active status. Penicillin exerts no demonstrable effect on acute epididymitis. When given intramuscularly, it produced no demonstrable improvement in 2 cases of gonorrheal rheumatism. Direct administration of 25,000 units of the drug quickly controlled the acute inflammatory manifestations in an acutely involved knee. Penicillin administered locally will cure some cases of anterior gonorrheal urethritis but is less effective than by the intramuscular route.

North Carolina Medical Journal, Winston-Salem

6:185-228 (April) 1945

Case Reports Broaden Tumor Clinic's Usefulness by Critical Analyses of Trends in Diagnosis and Treatment of Cancer. F. R. Lock and Martha D. Yow.—p. 185.
Principles Frequently Neglected in Treatment of Pollinosis. R. V. Ellis.—p. 190.
Significance of Pleurisy With and Without Effusion. A. L. Ormond.—p. 194.
Usefulness of Repeated Ophthalmoscopic Examinations During Treatment of Hypertension. F. W. Stocker.—p. 198.
Need for Widespread Whooping Cough Immunization. R. B. Lawson.—p. 201.

Public Health Reports, Washington, D. C.

60:429-456 (April 20)1945

Physical Impairments of Members of Low Income Farm Families—11,490 Persons in 2,477 Farm Security Administration Borrower Families, 1940: III. Impaired Hearing for Speech. Mary Gover and J. B. Yaukey.—p. 429.
Procedure for Handling of Field Samples of Dust and Fume. H. E. Seifert, R. G. Keenan and L. T. Fairhall.—p. 441.

60:457-484 (April 27) 1945

Over the Horizon in Public Health. T. Parran.—p. 457.
Extended Malaria Control Program. L. L. Williams Jr.—p. 464.

60:485-512 (May 4) 1945

Control of Rat Fleas (Xenopsylla Cheopis) by DDT. D. E. Davis.—p. 485.
Two-Cavity Dust Counting Cell. W. E. McCormick.—p. 489.

60:513-544 (May 11) 1945

Nontuberculous Pulmonary Calcification and Sensitivity to Histoplasmin. C. E. Palmer.—p. 513.
Studies of Acute Diarrheal Diseases: XIV. Clinical Observations. A. V. Hardy and J. Watt.—p. 521.

Review of Gastroenterology, New York

12:77-152 (March-April) 1945

*Study of Electrocardiogastrographic Test: Its Possibilities in Differentiating Benign or Malignant Gastric Changes. J. Menendez Feros.—p. 99.
Syphilis of Stomach: Case Report. F. H. Voss.—p. 111.
Peptic Ulcer: I. Etiology. R. Ehrmann.—p. 117.
Acute Bacillary Dysentery Due to Bacillus Alkalescens. W. Lieberman.—p. 123.

Electrocardiogastrographic Test.—According to Menendez Feros the electrocardiogastrogram is a clinical test by which one may measure the intragastric voltage obtained by an intragastric lead in connection with an electrocardiographic apparatus. He made 500 electrocardiogastrographic tests in the presence of normal and pathologic conditions. The test offers new aid in differentiating benign or malignant gastric changes and gives some idea regarding the metabolic changes of the gastric cells. These phenomena are considered to be related to the variations of the cellular permeability or surface tension which are connected with the electrical conductibility of the gastric cells. With the technic employed by the author, the ST segment and gastric T waves have a mean value of 0.3 cm. in healthy subjects. When the intragastric voltage of these waves is between 0.1 and 0 cm., severe gastric anatomic changes might be established. In cancer of the stomach the ST segment and T waves will frequently have a high voltage. These findings are more common in the malignant cases with a short period of evolution. When benign inflammatory changes are concomitant with the neoplasm, the intragastric voltage will be between these two opposite tendencies. In gastric cancer with a low intragastric voltage due to concomitant benign inflammatory changes an injection of epinephrine will increase the voltage. In normal cases or in pure benign inflammatory changes the epinephrine does not seem to have any electrical reaction; on the contrary, it has a tendency to decrease it. The same results have been obtained in gastric allergy.

United States Naval Med. Bulletin, Washington, D. C.

44:901-1124 (May) 1945. **Partial Index**

Casualty Handling Afloat: Practical Problems. G. R. Dunlop.—p. 901.
Casualties During Amphibious Combat Operation. N. H. Matros.—p. 909.
Medical Observations on Seabees in Jungle. N. L. Mistachkin.—p. 916.
Silk Technic in Appendectomy. P. Shambaugh.—p. 932.
Cotton Suture Material in Hernial Repair. N. E. Bear.—p. 939.
Surgical Treatment of Posttraumatic Painful Extremity. M. H. Brown. —p. 942.
*Pellegrini-Stieda Disease. E. J. Buckley.—p. 947.
Tyrothricin Therapy in Postoperative Pilonidal Cysts. H. Berger. —p. 952.
Pathologic Aspects of Appendix in Military Personnel. M. C. Wheelock. —p. 957.
Hyaluronic Acid: Tissue Polysaccharide: Some Effects on Erythrocytes. C. L. Spingarn and J. P. Jones.—p. 963.
Erythema Multiforme: Study of 10 Cases. W. W. Duemling and T. A. Lesney.—p. 968.
Pneumonia in U. S. Navy—1882-1942: Part I. As Cause of Admission to Sick List. D. F. Smiley and H. A. Raskin.—p. 973.
Streptococcic Pneumonia. E. B. Erskine.—p. 985.
Oxygen Concentration in Oxygen Tents. Margaret H. Wolff.—p. 988.
*Treatment of Malaria with Arsenicals. W. H. Stewart.—p. 991.
Peptic Ulcer in Naval Personnel. M. M. Baumgartner.—p. 995.
Intravenous Salicylates in Rheumatic Fever. K. E. Martin.—p. 1000.
Prostatitis and Seminal Vesiculitis as Common Causes of Backache. W. H. Mast and W. C. Hurly.—p. 1002.
Urinary Frequency Among Personnel at Sea. C. A. Macgregor.—p. 1007.

Pellegrini-Stieda Disease.—Buckley states that a history of injury to the knee joint followed by pain, swelling, tenderness in the medial aspect and restricted motion of the joint is an indication that the Pellegrini-Stieda syndrome is present. This pathologic condition should be considered in cases of sprains or contusions if the aforementioned symptoms are present beyond the usual period of recovery. Serial x-ray studies should be made in all such cases. Many months after the initial injury complaint may be made of limitation of motion and weakness and discomfort of the leg, causing a disturbed function. Secondary arthritic changes may also be present. Early cases show a swelling of the soft tissues at the inner aspect of the knee. Several weeks later a calcified mass will be noted on palpation. The calcification, if present, is firm and slightly movable but not adherent to the overlying skin. The x-ray shadow is usually directed vertically in a crescentic shape, lying adjacent to the medial femoral condyle, with a soft tissue gap between the calcification and the distal end of the femur. The lesion is best seen in the conventional anteroposterior view. The histories of the 2 patients are illustrated by roentgenograms showing the crescentic calcification in the region of the adductor tubercle.

Treatment of Malaria with Arsenicals.—Stewart treated 78 malarial survivors of a naval engagement who had tertian malaria. All had been exposed to the bite of malaria-carrying mosquitoes. They had no mosquito netting and no prophylactic medication for the fifteen days they were ashore. Immediately after being evacuated, all were given suppressive therapy consisting of 0.2 Gm. of atabrine on alternate days. The first case of malaria appeared five days later, and new ones continued to develop during the following fortnight. A routine method of treatment was adopted which consisted of bed rest and 0.65 Gm. of quinine sulfate three times daily. In a group of 10 patients who had been tried on quinine with unfavorable results, oxophenarsine hydrochloride 0.04 Gm. was given in addition to the quinine. The oxophenarsine hydrochloride was administered intravenously in a single dose to those men who had continued to have high temperatures after at least three or four days of quinine therapy. In all but 1 the temperature fell to normal within a few hours after the oxophenarsine hydrochloride injection and did not subsequently rise above 99 F. Seeing the excellent results obtained in these 10 cases, it was decided to try oxophenarsine hydrochloride on 3 unselected patients. In none of these 3 patients did fever appear subsequently, so that it became possible to put them on ambulatory treatment after only four days in the sickbay. The average hospital period of the 10 quinine resistant cases after treatment with oxophenarsine hydrochloride was three and one-half days. Reactions to oxophenarsine hydrochloride are rare. It is probably advisable to use at least four injections of 0.04 Gm. at weekly intervals following the initial treatment.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

Australian and New Zealand J. Surgery, Sydney

14:147-216 (Jan.) 1945

Recent Investigations Concerning Biochemistry of the Thyroid Gland. V. M. Trikojus.—p. 147.
*Removal of Blood from Traumatic Hemothoraces. T. I. Hayward. —p. 157.
Review of Present Surgical Treatment of Peptic Ulcer and Carcinoma of Stomach. J. B. G. Muir.—p. 173.
Early Treatment and Results of Penetrating Wounds of Chest: Further Report. C. W. B. Littlejohn.—p. 194.

Removal of Blood from Traumatic Hemothoraces.—Extravasated blood in the pleural cavity acts as an irritant and causes an inflammatory response in the pleura. Inflammatory exudate seeps into the pleural cavity diluting the blood, and fibrous tissue commences to grow. Great fibrous thickening and even calcification of the pleura may result with prolonged or permanent respiratory disability. When the blood is efficiently removed many patients will have a dry and healed pleura within a month with no respiratory disability remaining, and those who become infected will have a small loculated empyema instead of one coextensive with the original hemothorax plus the added exudate. Treatment by repeated aspirations fits into the plan of dealing with hemothoraces in New Guinea. The needle must be of adequate bore and length. Aspiration is repeated every three days until the pleura is dry, but the interval is varied to suit each case and usually becomes longer as the effusion becomes smaller. It is a common fault to carry out aspiration at too low a level. The needle should rarely be inserted below the ninth intercostal space just medial to the angle of the scapula, the eighth just lateral to the angle of the scapula, the seventh in the posterior axillary line (usually the best to try first), the sixth in the midaxillary line, the fifth in the anterior axillary line and the fourth in the nipple line. Inexperienced men may fail because the needle enters the phrenicocostal sinus and pierces the diaphragm. It is advisable to aspirate all the fluid which can be obtained, but removing more than a pint is inadvisable because sudden and large changes in the degree of aeration or collapse in the lung should be avoided.

British Medical Journal, London

1:399-432 (March 24) 1945

Therapeutic Trial of Methionine in Infective Hepatitis. C. Wilson, M. R. Pollock and A. D. Harris.—p. 399.
*Treatment of Infective Hepatitis with Methionine. G. Higgins, J. R. P. O'Brien, R. A. Peters, Alice Stewart and L. J. Witts.—p. 401.
Antidiuretic Action of Nicotine and of Smoking. J. H. Burn, L. H. Truelove and Isabel Burn.—p. 403.
Enforced Leisure: Study of Activities of Officer Prisoners of War. A. R. Dearlove.—p. 406.
Substances Used in Treatment of Pediculosis Capitis: Their Relative Value. Elizabeth B. S. Scobbie.—p. 409.
Local Effects of Intramuscular Injection of Solvochin. F. Hawking. —p. 412.

1:433-470 (March 31) 1945

Imbalance of Vitamin B Factors: Pyridoxine Deficiency Caused by Additions of Aneurin and Chalk. M. B. Richards.—p. 433.
Duct Papillomata of Breast: Plea for Conservative Treatment. C. P. G. Wakeley.—p. 436.
"Neutral Proflavine Sulfate" (Monosulfate of 2: 8-Diaminoacridine): Its Local Action in Infected Wounds Involving Bone. J. F. Heggie, G. B. R. Warnock and R. W. Nevin.—p. 437.
Hereditary Hemorrhagic Telangiectasis. D. Cappon.—p. 440.
Newer Concepts of Breast Feeding. M. Witkin.—p. 441.
Unilateral Hypotony During Anesthesia. Ina Brittain and G. J. C. Brittain.—p. 442.
Psychologic Reactions in the Wounded. L. Minski.—p. 444.

Methionine in Infective Hepatitis.—Higgins and his associates administered methionine to alternate patients with infective hepatitis. The total number was 37, of ages between 17 and 45 years. Care was taken to exclude patients with liver disease from other causes; no patient who had received neoarsphenamine or who had been exposed to any toxic substance was included in the experimental group. The patients were kept in bed. To minimize the chance variation of the methionine content of the meals, all patients, treated and untreated, were put on a diet of low fat and high protein content, supple-

mented with vitamins. A record was kept of the amount eaten by every patient at each meal. It was estimated that the methionine content of the diet consumed daily was of the order of 2.5 Gm. Throughout the day five 1 Gm. doses were given either in milk or after flavoring with fruit juice. Including that in the diet, the treated patients received daily nearly 7.5 Gm. of methionine. Treatment with methionine did not significantly affect the clinical course of the illness, the anorexia or the average duration of biliuria or of bilirubinemia.

1:471-504 (April 7) 1945

*Control of Infection in Recent Wounds by Surgery and Local Chemotherapy. F. H. Bentley and S. Thomson.—p. 471.
Blast Injury to Lungs: Clinical and Radiologic Findings and Their Relation to Certain Symptoms. G. R. Fearnley.—p. 474.
Outbreak of Jaundice with Signs in Nervous System. E. A. J. Byrne and G. F. Taylor.—p. 477.
Social Study of Hospital Treatment. M. Brown and F. C. Carling.—p. 478.
Pulmonary Acariasis in Monkeys. L. J. Davis.—p. 482.
Fulminating Gas Gangrene: Fatal Case with Unusual Accompanying Features. C. J. Cellan-Jones and E. M. Griffin.—p. 482.

Control of Infection in Wounds.—Bentley and Thomson, members of the penicillin control team in the Central Mediterranean Force, investigated the value of sulfanilamide and penicillin when applied locally in the treatment of recent wounds. In an investigation of 1,000 wounds during the battle for the Gothic Line the organism of initial sepsis was found to be Staphylococcus pyogenes aureus. The incidence of infection in wounds before operation at the casualty clearing station was about 51 per cent. In wounds undisturbed during transit and treated at the casualty clearing station by operation alone, 49 per cent were infected and 23 per cent were septic; by operation and sulfanilamide powder, 43 per cent and 11 per cent; by operation and penicillin-sulfathiazole powder, 25 per cent and 7 per cent, when examined in the base hospital five to ten days later. Thus operation alone did not completely remove infection from a recent wound. Sulfanilamide applied locally had a bacteriostatic effect; for although the infecting bacteria persisted, their activity was depressed, so that the incidence of sepsis was reduced. Penicillin-sulfathiazole powder similarly applied was more effective; its use was followed by the destruction of the infecting cocci in about one half of the infected wounds with an equally low incidence of sepsis. Wounds operated on at the casualty clearing station in under twelve hours had a lower incidence of infection than those operated on between twelve and twenty-four hours in all the chemotherapy groups. Wounds that had been redressed between casualty clearing station and base hospital had a higher incidence of infection than had those that had not been disturbed. The importance of control of infection by operation and chemotherapy at the casualty clearing station is illustrated by the results of suture. Of wounds uninfected with pyogenic organisms 80 to 85 per cent obtained grade 1 union, whether appearing clean or dirty, whereas wounds that were infected, even if appearing clean, showed a lower rate of success.

1:505-544 (April 14) 1945

Recent Work on Pharmacology of Sulfonamides. F. Hawking.—p. 505.
Investigation and Results of Treatment of 1,000 Cases of Vaginal Discharge. O. Lloyd.—p. 509.
*Treatment of Epilepsy by Electrically Induced Convulsions: Preliminary Report. G. Caplan.—p. 511.
Fractures of Zygoma Bone. B. Elizabeth Nesbitt and C. R. D. Leeds.—p. 512.
Solitary Diverticulum of Cecum. G. C. Dorling.—p. 513.
Penicillin and Fibrinolysis. K. Dixon.—p. 514.

Electric Convulsions in Epilepsy.—Caplan regards epilepsy as a disturbance of the electrical equilibrium of the brain which leads to the occasional accumulation of an excessive quantity of energy. The epileptic fits can be regarded as a discharge mechanism whose function it is to disperse this energy whenever it exceeds a certain threshold value. An epileptic patient's chief disability lies in the fact that his fits are rarely predictable and may occur at any awkward moment or in situations involving considerable danger. The idea has therefore been developed of replacing these spontaneous fits by electrically induced convulsions which can be produced under controlled conditions of time and place. This therapy should not supersede the pharmacologic methods of combating the fits, but rather it should be an accessory treatment in those cases in which fits occur despite full dosage of anticonvulsant drugs. This paper is a preliminary report on 15 cases of epilepsy in which electrical convulsions were tried. In 11 cases the fits have been materially diminished. In 7 cases the symptoms of an associated psychosis have been ameliorated. The value of an induced convulsion as a means of terminating a dangerous psychic equivalent has been illustrated. No serious or alarming complications have been experienced.

Edinburgh Medical Journal

32:61-96 (Feb.) 1945

Meningococcal Endocarditis: Review. W. R. Logan.—p. 49.
Management of Multiple Injuries in Airerews. I. L. Dick.—p. 61.
Investigations of Vitamin A Content of Human Body Fluids. W. Tomaszewski and L. Dziatoszyński.—p. 74.
Wilson's Disease. A. J. Glazebrook.—p. 83.

Journal of Pathology and Bacteriology, Edinburgh

57:1-156 (Jan.) 1945

Bacteriophage Action on Bact. Typhosum and B. Megatherium as Displayed by Dark Ground Cinemicrography. A. Pijper.—p. 1.
Tissue Changes in Experimental Mice Treated with Pentose Nucleotides. L. Dorothy Parsons.—p. 9.
Phagocytosis of Vaccinia Virus in Vitro. K. B. E. Merling.—p. 21.
Bacterial Flora of Wounds and Septic Lesions of Hand. R. E. O. Williams and A. A. Miles.—p. 27.
Study of Effects of Applying Pressure to Experimental Thermal Burns. G. R. Cameron, J. W. Allen, R. F. G. Coles and J. P. Rutland.—p. 37.
*Bacteriologic Aspects of Penicillin Therapy. F. R. Selbie, Rosemary D. Simon and J. McIntosh.—p. 47.
In Vitro Determination of Sulfonamide Sensitivity of Bacteria. G. J. Harper and W. C. Cawston.—p. 59.
Notes on Examination of Exudates for Pathogenic Anaerobes. W. J. Tulloch.—p. 67.
In Vitro Production of Alpha Toxin, Theta Hemolysin and Hyaluronidase by Strains of Cl. Welchi Type A, and Relationship of In Vitro Properties to Virulence for Guinea Pigs. D. G. Evans.—p. 75.
Lipids of Human Kidney Cortex and Medulla in Fatty Change. G. Popják.—p. 87.
Observations on Anti-Pernicious Anemia Factor, with Suggested Method for Testing Liver Extracts in Laboratory. W. Jacobson, H. Stewart and S. M. Williams.—p. 101.
Isoagglutinin Titers in Heterospecific Pregnancy. G. H. Smith.—p. 113.
Nonhemolytic Group K Streptococcus from a Case of Endocarditis. J. L. Penistan.—p. 123.
*Life Span of Red Cell in Man. S. T. Callender, E. O. Powell and L. J. Witts.—p. 129.

Bacteriologic Aspects of Penicillin Therapy.—Research on the clinical application of penicillin gave Selbie and his associates the opportunity of studying this subject from the bacteriologic point of view. They found that Staphylococcus aureus is in the great majority of cases sensitive to penicillin, but variation was shown in the degree of sensitivity: 15 of 157 strains were at least eight times less sensitive than the standard strain. Streptococcus pyogenes and pneumococci were usually sensitive and showed only minor variation in susceptibility. Some of the nonhemolytic streptococci showed considerable resistance. The 10 strains of Actinomyces were less sensitive than the Oxford staphylococcus, but the majority were within the therapeutic range of penicillin. Observations on penicillin blood levels indicate that a dose of 20,000 units given intramuscularly every three hours will maintain a bacteriostatic concentration sufficient to deal with all sensitive organisms likely to be encountered. The penetration of penicillin from the blood into cavities and in particular the subarachnoid spaces (cerebrospinal fluid) is at times insufficient and has to be supplemented by direct injection. A good indication of improvement in pyogenic infections is a diminution in the blood leukocyte count. The rate of disappearance of the micro-organisms depends largely on the nature of the lesion. In acute infections they disappear as a rule in a few days but persist longer in deep foci and in areas of devitalized or necrotic tissue. This persistence is especially characteristic of lung infections, where they appear to have a purely saprophytic existence. Secondary invasion by penicillin insensitive organisms is liable to occur, especially in wounds sustained in battle or in air raids. The development of resistance to the drug was observed in a small number of instances.

Life Span of Red Cell.—Callender studied the survival of transfused erythrocytes in 3 normal male subjects of group A from whom blood was removed and replaced by blood of group O. The curve of decay of the transfused cells was linear within the experimental error; their average life was sixty days. The relation between the decay of transfused cells and the law of survival of the individual erythrocyte has been deduced. It is concluded that red cells live for one hundred and twenty days in men, which is the true average life. The normal rate of replacement is 0.83 per cent daily.

Journal of Physiology, Cambridge

103:359-488 (March) 1945

Glycogen in Adipose Tissue. E. Wertheimer.—p. 359
Synthesis of Acetylcholine by Tissue of Central Nervous System. W. Feldberg.—p. 367.
Excitability Changes at Neuromuscular Junction During Tetany. S. W. Kuffler.—p. 403.
Effect of Initial Level of Blood Pressure on Response of Human Subject to Blood Pressure Raising Reflexes. M. B. Bruce, R. T. Martin and F. H. Smirk.—p. 412.
Respiration and Cardiac Output in Isolated Heart-Lung-Head Preparation in Rat. E. W. H. Cruickshank.—p. 417.
Facilitation, Inhibition and Depression at Artificial Synapse Formed by Cut End of a Mammalian Nerve. R. Granit and C. R. Skoglund. —p. 435.
Mechanism of Water Diuresis in Normal Rats and Rabbits as Analyzed by Inulin and Diodone Clearances. S. E. Dicker and H. Heller. —p. 449.
Observations on Thermal Burns: Influence of Moderate Temperature Burns on a Proteinase of Skin. A. Beloff and R. A. Peters.—p. 461.
Activity of Vagal Stretch Endings During Congestion in Perfused Lungs. E. Bülbring and D. Whitteridge.—p. 477.

Lancet, London

1:359-390 (March 24) 1945

Hunterian Museum: Yesterday and Tomorrow. G. G. Turner.—p. 359.
Psychiatric Casualties Among Officers and Men from Normandy: Distribution of Etiologic Factors. E. Miller.—p. 364.
Repair of Perforating Corneal Wounds. R. A. D. Crawford.—p. 366.
Penicillin Gonorrhea: Suggested Scheme of Treatment. T. R. L. Jones, F. G. Maitland, S. J. Allen, with a Postscript by S. Dudley. —p. 368.
Rehabilitation in Naval Hospital. H. J. Burrows.—p. 370.

1:391-422 (March 31) 1945

Resettlement of Disabled in Work. T. Ferguson.—p. 391.
Are Sulfonamides Merely Bacteriostatic Agents? L. Colebrook and W. C. Cawston.—p. 394.
*Penicillin in Clostridial Infections: G. H. Fisher, M. E. Florey, T. A. Grimson and P. M. De C. Williams.—p. 395.
Subcapital Fractures of the Femoral Neck Fixation by Pin and Graft. E. N. Wardle.—p. 399.
Multiple Attacks of Cerebrospinal Fever. W. F. Corfield.—p. 402.
Mikulicz Pack Used in Thoracic Wound. A. R. Clarke.—p. 403.

Penicillin in Clostridial Infections.—During the first weeks after D day Fisher and his associates made observations on the influence of penicillin on the incidence and course of gas gangrene and allied conditions. Penicillin should prevent the development of gas gangrene rather than treat the established condition. Inadequate "prophylactic" administration may lead to a serious clinical picture very different from that associated with either gas gangrene or anaerobic cellulitis. During the period June 8 to July 24, 3,907 battle casualties were admitted; 436 of these had been treated with injections of penicillin. These were those most liable to suffer from gas gangrene. The treatment prescribed was an initial injection of 100,000 units, followed in about six hours by 45,000 to 50,000 units at four or five hour intervals till definitive surgical treatment could be carried out. Had the selection been perfect, cases of gas gangrene and allied conditions should not have developed in those not prophylactically treated with penicillin, but such conditions developed in 28 out of a total of 3,471 cases; among these 28 were 5 cases of gas gangrene. Among the 436 prophylactically treated with penicillin 2 developed "gas" infection but none had gas gangrene. The authors discuss four groups of cases. The first group includes those first recognized as gas infection in the emergency hospital, the second group those recognized and treated before; in the two other groups gas infection was not diagnosed, but those of the third group had dirty lacerated wounds and were treated earlier with prophylactic penicillin; those of the fourth group had "clean" lacerated wounds. The diagnosis of gas infection was made on the basis of the following clinical criteria: swelling and color of muscles, thin brownish discharge, presence of gas, smell, discoloration of surrounding skin, and general condition of the patient. None of the cases of the first group had reached the stage of fulminating gas gangrene. They would be classified as "anaerobic cellulitis" or "local gas gangrene" of muscle. Bacteriologic diagnosis was made both on film and in culture. Both supported the diagnosis. The following therapeutic program was found most satisfactory: immediate injection of 20,000 units of penicillin, repeated at the beginning of operation and thereafter three hourly or by intramuscular drip, for from ten to fifteen days. Immediate injection of 50 to 100 thousand units of gas gangrene antiserum, repeated if considered necessary. Wide incision of the wound and excision of only definitely necrotic muscle. The lengthy penicillin treatment was thought necessary owing to the observation that the swelling of muscles, clostridial infection and evidences of toxemia persisted much longer than the unhealthy appearance of the muscle surfaces. As a precaution against secondary infection, penicillin paste, 250 units per gram, was applied locally as soon as systemic treatment was discontinued and till secondary suture or skin grafting could be carried out. Patients liable to develop gas gangrene should receive a penicillin injection as soon as possible after wounding, and treatment should be continued till granulations have formed on the wound surface. With a short or interrupted course of penicillin a profound or protracted toxemia may result in spite of the absence of typical local signs. In such cases the diagnosis may be missed and the patient fail to receive further penicillin or gas gangrene antiserum.

Medical Journal of Australia, Sydney

1:265-288 (March 17) 1945

Observations on Certain Bacteriologic and Serologic Examinations of Stored Blood. Marjorie Bick.—p. 265.
Aspiration Biopsy. T. E. Wilson.—p. 268.
*Experimental Transfusion with Malaria Infected Blood. R. Officer. —p. 271.
Experimental Observations on Limitations of Oil as Vehicle for Anesthetic Agents. M. Kelly.—p. 274.

Transfusion with Malaria Infected Blood.—Officer says that the use of potentially malaria infected individuals as donors for blood transfusion has been regarded as dangerous heretofore because the patient might develop malaria, but in an emergency it would be foolish to deny the benefit of transfusion to an exsanguinated patient if the malarial parasites so transmitted could be dealt with effectively by doses of quinine. Experimental transfusions of malarial blood containing large numbers of parasites have been carried out on 5 volunteer recipients. One volunteer had two such transfusions. The transfusions were immediately followed by routine antimalarial treatment. The author concludes that the development of malaria in a nonimmune recipient following blood transfusion from an infected donor can be prevented by the immediate institution of antimalarial therapy. In case of emergency a potentially malarial donor could be used for transfusion, with the knowledge that the benefit derived from the transfusion would far outweigh any ill effects resulting therefrom.

South African Medical Journal, Cape Town

9:33-48 (Feb. 10) 1945

A Physician's Visit to Central Africa. J. F. Brock.—p. 34.
Mortality from Cancer in England and Wales Viewed from New Angle. C. Pijper.—p. 39.
Successful Response to Penicillin in Case of Subacute Bacterial Endocarditis. B. G. Shapiro.—p. 40.
*Case of Ovalocytosis. J. Barnetson.—p. 42.
Actinomycosis Treated with Sulfonamides. C. A. H. Watts.—p. 43.

Case of Ovalocytosis.—Barnetson reports the history of a middle aged woman of European extraction who was hospitalized with symptoms suggesting chronic colitis. During a routine blood count it was discovered that 95 per cent of the erythrocytes were oval. The patient had no history of anemia, nor did the family history reveal anemia. Examination of the blood of a brother revealed that 45 per cent of the erythrocytes were oval. Ovalocytosis is an unusual and interesting abnormality of the blood. It is never associated with noteworthy anemia, and it is not related to sickle cell anemia in Negroes.

Archiv für klinische Chirurgie, Berlin

205:549-818 (May 18) 1944. **Partial Index**

*Causation of Adhesive Pericarditis and Results of Its Surgical Treatment. H. H. Westermann.—p. 549.
*Is There Such a Condition as Wartime Toxic Diffuse Goiter? W. Gattig.—p. 580.
Results of Hochenegg's Method of Surgical Treatment for Cancer of the Rectum During the Period of 1900 to 1942. E. Fenster and K. O. Herrmann.—p. 589.
Surgical Treatment of Paralysis of Facial Nerve. H. von Seemen.—p. 598.
Late Stage of Infected Cranial Impression Gunshot Injury, Its Clinical Aspect and Its Treatment. T. Riechert.—p. 603.
Roentgenologic Demonstration of Duodenal Papilla. H. Beulin.—p. 636.
Therapy of Idiopathic Dilatation of Common Bile Duct (Congenital Coledochus Cyst). H. Michel.—p. 644.
Clinical Aspect of Tuberculosis of Kidneys. H. J. Lauber and G. Röhrs.—p. 668.

Adhesive Pericarditis.—Westermann reports results of surgical treatment in 53 cases of adhesive pericarditis. Rheumatism rather than tuberculosis plays the most important part in the genesis of the condition. The etiology is determined by the history and the postoperative course rather than by microscopic findings. The incidence of adhesive pericarditis may be reduced and the surgical treatment made more effective by combating the rheumatic infection. Of the patients 37 were male and 16 female; 15 were between the ages of 11 and 20 years, 19 patients between 21 and 30 years. The second and third decades of life show the highest incidence. Conservative treatment proved ineffective. Pericardiectomy was performed in all of the cases except 1, in which Brauer's operation was first performed. A two stage pericardiectomy by combining the transthoracic and the anterior fenestration method was performed in 2 cases. A large anterior window-like opening with a lateral pedunculated flap after Kocher was used in the one stage pericardiectomy in all the other cases. Complete recovery took place in 19 cases and considerable improvement in 15. The mortality rate was 35.8 per cent. Recovery and improvement in two thirds of the cases is to be considered as a highly satisfactory result in spite of the still high mortality rate. New adhesions from regenerating ribs and the systolic drawing in of the thorax may be prevented by the complete removal of the posterior periosteum of the ribs and by covering the heart with a soft cutaneous muscle flap. Precardiac cardiolysis may be combined with radical excision of the pericardium. This specific combination is to be considered as the essential factor on which the permanent results depend. Cooperation of the surgeon with the internist is important, since even better results may be obtained from pericardiectomy when performed in an early stage of the disease.

Wartime Toxic Diffuse Goiter.—Wartime toxic diffuse goiter does not represent a specific form of toxic diffuse goiter as to origin, clinical aspect, treatment or prognosis. A single physical exertion or a single instance of mental excitement, as well as prolonged mental or physical strain continuing for weeks or months, may be the eliciting factor in soldiers and in civilians alike. Toxic diffuse goiter must have been latent in these persons, since a specific change in the thyroid depending on an individual predisposition is to be considered as the principal cause of the disease. The incidence of fully developed toxic diffuse goiter was low during the first world war and has proved the same during the present conflict. The incidence of mild forms has been high, and differential diagnosis from purely nervous heart disorders and disturbances of circulation may be difficult. As observed by Gattig, in 4 of 5 soldiers the toxic diffuse goiter presented a gradual development of medium severity within one year. In the fifth soldier the sudden onset of the disease could be traced to the fact that he was buried under the falling fragments of a shelter which had been hit by an artillery shell. In 3 civilian patients the night bombardment of their homes was the eliciting cause of the disease, which developed within a few days after the bombardment. A mortal fear reaction however was missing at least in 1 instance in which the patient immediately regained his self control by helping to save other persons from the wreckage. Treatment of wartime toxic diffuse goiter does not differ from the usual treatment, but the results of Plummer's treatment, as well as the recovery rate, are less satisfactory in secondary toxic diffuse goiter in wartime than in primary toxic diffuse goiter.

Acta Medica Scandinavica, Stockholm

117:417-590 (Aug. 16) 1944. **Partial Index**

*Intrasternal Administration of Heparin. S. Lindgren and L. Walldén.—p. 417.
*Paroxysmal Paralytic Hemoglobinuria. A. Louw and H. E. Nielsen.—p. 424.
Pain and Rectal Tenesmus After Injection of Epinephrine into Colon. G. C. Brun.—p. 448.
Combination of Diabetes Mellitus and Acute Hepatitis. K. A. Vannfält.—p. 462.
Circulation in Fallot's Tetralogy. P. Eskildsen.—p. 488.
Investigations on Ascorbic Acid Content in Serum from Patients Suffering from Peptic Ulcer. I. Ebbesen and M. Rasmussen.—p. 507.
Reexamination of Patients with Exophthalmic Goiter Treated Conservatively. K. Brøchner-Mortensen and H. Uhrbrand.—p. 513.
Sedimentation Rate and Room Temperature. T. Romanus.—p. 535.

Intrasternal Administration of Heparin.—Lindgren and Walldén administered 57 mg. of heparin regularly at six hour intervals by intrasternal injection and found that the effect on the coagulation time was the same as when it was given intravenously. In view of the need of repeated injections, the needle can remain in the sternum; this is much easier than to keep a needle fixed in the cubital vein. The intrasternal method is recommended as an improvement in technic.

Paroxysmal Paralytic Hemoglobinuria.—Louw and Nielsen differentiate between exogenous and endogenous forms of hemoglobinuria. With the endogenous forms they group cold hemoglobinuria, march hemoglobinuria, chronic hemolytic anemia (Marchiafava type) and paralytic hemoglobinuria or myoglobinuria. This last form is rare, only 4 cases having been reported previously. After reviewing these cases, the authors describe myoglobinuria in a boy aged 10 who had a history of repeated attacks of muscular pain and difficulty in walking since the age of 4 years. During an acute attack, when the boy was admitted to the hospital, the urine was dark reddish brown and gave a strong reaction for blood. Spectroscopic analysis showed that myoglobin was excreted in the urine during the attack, at which time there was also creatinuria. The boy was feeling well at his discharge. The appearance of 8 cases of progressive muscular dystrophy in the family of this boy suggested that progressive muscular dystrophy and paralytic myoglobinuria may be different forms of the same disease, the latter representing the acute manifestation of the lesion, while progressive muscular dystrophy is the chronic form.

Nordisk Medicin, Stockholm

21:189-244 (Feb. 4) 1944. **Partial Index**

Blood Donor Activity of Health Board. O. Nordlander.—p. 189.
Pemphigus Contagiosus of Newborn, Especially with Regard to Prophylaxis and Treatment. O. Kaalund-Jørgensen.—p. 196.

Hospitalstidende

New Instrument for Wire Extension. E. Madsen.—p. 199.

Hygiea

*Thrombophlebitis Saltans: Case. E. Feltström.—p. 217.
Osteosynthesis with Kirschner's Thread. J. Cedermark.—p. 219.

Thrombophlebitis Saltans.—In Feltström's case of venographically verified thrombosis in the right leg and thigh the course was normal for a few days after heparin treatment, but new disturbances atypical both for thrombosis and for the usual banal thrombophlebitis affected in turn different segments of the walls in the deep veins in the right and left leg, with secondary thrombus formation. Heparin treatment at once stopped the fresh thrombotic process but seemed powerless against further spread of the pathologic process. Recovery resulted after treatment with injections of estrogen.

Svenska läk.-sällsk. förhandl.

*Etiology of Prostatic Hypertrophy from Endocrine Points of View. N. Törnblom.—p. 229.
Genesis of Detachment of Retina and Operative Treatment. R. Rosengren.—p. 239.
Ocular Complications in Sulfonamide Therapy. S. Holm.—p. 240.

Etiology of Prostatic Hypertrophy.—Törnblom says that it is uncertain whether hypertrophy of the prostate is due to endocrine disturbances. Endocrine treatment therefore is a shot in the dark. The favorable effects attributed to treatment with testosterone propionate may depend on a generally stimulating action of this preparation

Book Notices

Handbook of Physical Medicine. Selections Authorized for Publication by the Council on Physical Medicine, American Medical Association. Previous editions of this work were published under the title of Handbook of Physical Therapy. First edition. Cloth. Price, $2. Pp. 392, with illustrations. Chicago: American Medical Association, 1945.

The first edition of the Handbook of Physical Medicine is actually the fourth edition of the Handbook of Physical Therapy. It was prepared under the auspices of the Council on Physical Medicine of the American Medical Association. Physical medicine includes the diagnosis and treatment of disease by various nonmedical means. It employs the physical and other effective properties of light, heat, cold, water, electricity, massage, manipulation, exercise and mechanical devices for physical and occupational therapy in the diagnosis and treatment of disease.

The Handbook of Physical Medicine represents a summary of the efforts of the Council during a twenty year period to separate the beneficial from the useless in this form of therapy, to evaluate the various physical therapeutic agents and the methods of their employment and to protect the medical profession from the snares and pitfalls found in this field.

When Dr. Joseph F. Smith brought a resolution before the House of Delegates of the American Medical Association urging the Board of Trustees to establish a Council on Physical Therapy, the board chose nine men from the ranks of chemists, physicists, pathologists, physiologists, radiologists and clinicians to compose the Council. Later the membership was increased to twelve. In 1944 the Board of Trustees changed the name to the Council on Physical Medicine.

Many members of the medical profession, representing the various specialties, have acted as referees or consultants for the Council. These men have tested physical agents and apparatus submitted for acceptance, studying the therapeutic claims made for them, evaluating the merit of special articles submitted for publication and aiding in the educational work of the Council.

The Council's aims and purposes are threefold: 1. To protect the medical profession and thereby the public against inefficient and possibly dangerous apparatus and against misleading and deceptive advertising in connection with the manufacture and sale of devices for physical therapy. 2. To disseminate such reliable information as it possesses or may acquire and to stimulate instruction to aid the practicing physician in choosing true and sound physical therapeutic methods. 3. To act in an advisory capacity to the profession and to the public in all matters concerning this branch of medicine. The work of the Council has progressed along two distinct lines: 1. The evaluation of the efficacy of physical therapeutic apparatus, usually but not always submitted for Council consideration, through a study of the therapeutic claims made for such devices; the elimination of false, misleading or exaggerated statements in advertising matter concerning the equipment and the publication of the Council's acceptance or rejection of the given physical agent in THE JOURNAL. The booklet Apparatus Accepted can be obtained free of charge by writing to the Secretary of the Council. 2. The improvement of the type of physical therapy practiced by the profession.

Some of the subjects discussed are evaluation of methods used in physical therapy; physiologic effects of heat; heat in surgical and orthopedic conditions; fever therapy; physiology of massage; body mechanics and posture; therapeutic and remedial exercise; occupational therapy; hydrotherapy; colonic irrigation; electrical stimulation of muscle; medical diathermy; electrolysis; ultraviolet and infra-red radiation used in therapy; physical therapy in the treatment of fractures, in infantile paralysis, in psychiatric practice and in skin diseases.

Neuro-Ophthalmology. By Donald J. Lyle, B.S., M.D., F.A.C.S. Fabrikoid. Price, $10.50. Pp. 395, with 234 illustrations and 7 charts for recording lesions affecting the visual system. Springfield, Ill.: Charles C Thomas, 1945.

This work deals with the relationship of the eye to the brain, showing the effect of certain diseases of the brain on the eyes. An attempt is made to obviate the necessity of referring to the many textbooks on neurology so as to glean from here and there, with much time consuming effort, information pertaining to neuro-ophthalmology. The plan is to bring together in brief but comprehensive and coordinated manner those many phases of neurology as far as they concern, directly or indirectly, neuro-ophthalmology. The first twelve chapters are devoted to embryology, anatomy, pathology, physiology and morphology. The remaining seven chapters include a thorough discussion of the various infections, diseases and tumors that affect the brain and eye. The chapter on intracranial and orbital neoplasms is especially comprehensive, although no attempt is made to include a classification of brain tumors.

There are 130 necropsy or operatively confirmed case histories, which have been outlined in connection with the text. There are many retinal photographs of ocular conditions, about half of which are stereoscopic and so placed that one can observe them through the stereoscope in order to obtain depth perception. Several charts for recording lesions affecting the visual system are included. The final chapter includes a discussion on eye manifestations of head injuries, which should be of vital interest to every ophthalmologist. This book should be welcomed by many ophthalmologists, neurologists and neurosurgeons because this vast subject matter is correlated into a working unit.

A Textbook of Pathology: Pathologic Anatomy in Its Relation to the Causes, Pathogenesis, and Clinical Manifestations of Disease. By Robert Allan Moore, Edward Mallinckrodt Professor of Pathology, Washington University School of Medicine, Saint Louis. Cloth. Price, $10. Pp. 1,338, with 513 illustrations. Philadelphia & London: W. B. Saunders Company, 1944.

In writing a textbook of pathology, an author must ask himself "Is this a book for students?" or "Is it for practicing physicians?" or "for specialists in pathology?" The approach to these various avenues would imply stressing fundamental problems of interest to different groups. However, in recent years writers in the various branches of the medical subjects have sought to include and correlate the fundamental sciences as part of their discussion for a better understanding of disease problems. Anatomy, physiology, chemistry, bacteriology and pathology are the pillars supporting the framework about which the better understanding of the cause and effect, the pathogenesis and epidemiology of disease and the effectiveness of the therapy is better understood. Physicians today do not have to "guess" what the nature of the patients' ailments are, they need only evaluate the objective and subjective findings in terms of the basic sciences. Therapy should not be empirical but placed on a scientific level of understanding the reasons for the drug which is prescribed for the patient.

Moore has achieved some of these objectives. As he has indicated, his textbook on pathologic anatomy is presented in its relation to the causes, pathogenesis and clinical manifestations of disease. This is an excellent approach, for, as Moore has demonstrated in his book, pathology can and should be made dynamic. Gone is the era of the pure morphologist, the dead house pathologist; and this important subject of pathologic anatomy must be presented in an interesting, understanding and vital manner. The clinical pathology conferences, the surgical, neurologic and various other branches of medicine in which the clinician and pathologist meet to discuss their medical problems throughout hospitals and teaching institutions in this country are indicative of the cooperative manner in which physicians work for the benefit of their patients and the community. But to interest the clinical branches in medicine along this line of thinking it was necessary for the pathologist to make his branch of medicine a vital and integral part of the whole. The clinician thinks in terms of pathology, the pathologist analyzes and interprets his subject in terms of clinical medicine.

Moore has presented his material in an interesting manner. As a teacher in pathology he understands the needs of the student. This is manifest in his book by his arrangement of the subject matter according to the causative agent or agents. In a simple, concise and lucid manner the subject is discussed. Long, uninteresting discussions are eliminated for the sake of brevity. There is too much material presented for detailed review; the literature (mostly in English) at the end of the chapter can be further studied by the interested reader. If a disease is designated by the discoverer's name, Moore tells the reader who this person is or was. Virchow, Rokitansky, Koch,

Cohnheim, Bright, Councilman, Welch, Wells are not mere names; they mean something to the student who reads about the disease which these men have described. A discussion on physiologic alterations, chemical changes, bacteriologic factors is interwoven in the discussion, so that the student now has an understanding of the alterations in form and disturbances of function that take place in disease to prepare him for his better understanding of clinical medicine.

Moore also discusses deficiency diseases, tropical medicine, diseases of unknown or obscure cause and the virus diseases. Thus the practicing physician and specialist in pathology may find in this book information which will benefit him in his specialty.

We do not wish to imply that this textbook is the answer to all the problems in pathology for the clinician and the pathologist. There are several examples that one can cite that the reader may take exception to. To cite just one example, the histogenesis of tuberculosis is not complete; the formation of caseation necrosis and the mechanism of bone formation could be discussed in more detail. But these are minor compared to the overall subject matter presented. Practically every phase of pathology has been discussed, and in a textbook of pathology of this size some detailed phases must be eliminated for the sake of the overall subject matter.

The text is clear and the illustrations have been well selected. There is a good index. The book can be highly recommended and should be in the library of students, physicians and hospitals.

Tropical Nursing: A Handbook for Nurses and Others Going Abroad. By A. L. Gregg, M.A., M.D., M.Ch., Member of Associate Staff of Hospital for Tropical Diseases, London. Second edition. Cloth. Price, $3. Pp. 185, with 13 illustrations. New York: Philosophical Library, 1944.

Some of the most important information in this handbook is included in the introduction and the chapter on personal hygiene in the tropics. The advice offered to one going to the tropics for the first time is sound and might well be heeded. The diseases are treated briefly and in an elementary fashion. The descriptions are hardly complete enough for the nurse to risk a differential diagnosis and start treatment in the absence of a doctor. The nursing procedures referred to are all ones employed in illnesses of temperate climates and in effect deny the existence of a field of "tropical nursing." However, the important part that insect vectors play in transmission of tropical diseases is aptly stressed with its relation to the nursing problems. A section on technic which outlines blood examination, blood transfusion, bowel lavage, the test meal, intramuscular injection and intravenous injection is a simple review for handy reference. The section on care of the eyes in the tropics includes injury from intense sunlight and that due to insects. The glossary of tropical terms contains few terms restricted to tropical medicine. A table of weights and measures is included for reference purposes.

Textbook of Anaesthetics. By R. J. Minnitt, M.D., D.A., Director of Anaesthetics, David Lewis Northern Hospital, Liverpool, and John Gillies, M.C., M.B., Ch.B., Consultant in Anaesthetics, Department of Health for Scotland. With a chapter on Local and Regional Analgesia by L. B. Wevill, M.B., F.R.C.S., Major R. A. M. C., which includes a section on Its Application to Dentistry by Dr. John Boyes, Dental Surgeon in charge, Facio-Maxillary Unit, Bangour E. M. S. Hospital, Scotland. Sixth edition. Cloth. Price, $7. Pp. 487, with 199 illustrations. Baltimore: William Wood & Company, 1944.

The former "Handbook of Anaesthetics" by Ross and Fairlie was revised in a fifth edition in 1940 by R. J. Minnitt. This, the sixth edition, has been rearranged and largely rewritten by R. J. Minnitt of Liverpool and John Gillies of Edinburgh. The scope of the book has been considerably extended to conform to the change in name to "Textbook of Anaesthetics." In general, the authors are to be congratulated on the changes and additions. It is now a book which probably is honestly and fairly representative of the thought and practice among a majority of British anesthetists. Certain points of disagreement with the opinions held in this country are present and to be expected. That the effort deserves to be called a textbook of anesthetics would be questioned by many. As a pleasant and profitable means of familiarizing oneself with modern British practice in anesthesiology, it should prove useful to the medical profession in this country.

The Foetal Circulation and Cardiovascular System, and the Changes That They Undergo at Birth. By Alfred E. Barclay, O.B.E., D.M., F.R.C.P., Kenneth J. Franklin, D.M., F.R.C.P., and Marjorie M. L. Prichard, M.A. Cloth. Price, 50s. Pp. 275, with 160 illustrations. Oxford: Blackwell Scientific Publications, Ltd., 1944.

Seven years ago Dr. A. E. Barclay, the dean of British roentgenologists, decided to tackle the problem of determining exactly what happens in the circulation when a placental animal is born; he wanted particularly to determine the time of functional closure of the ductus venosus. In order to facilitate this research, Dr. Barclay devised a cineradiographic apparatus and joined forces with Dr. Kenneth J. Franklin and Marjorie M. L. Prichard.

The book which describes their studies begins with a fine chapter on the history of the problem and what has been learned —mainly by the anatomists and embryologists. The next chapter is on the course of the blood flow in the fetal animal—mainly the lamb—as determined with the help of cineradiography and an opaque medium in the blood vessels. Chapter III reports a detailed study of the behavior of the many parts of the cardiovascular system in the mature fetal lamb. Chapter IV is on the circulation of the mature fetal lamb and the respiratory mechanisms which take over after birth. Chapter V is on lambing as it is observed by shepherds. Chapter VI is on the changes which occur during and shortly after the birth of the lamb. These changes are listed in approximate order on pages 126 and 127. The exact order has not yet been established for all the changes, but the authors have evidence for the view that there is a functional closure in the ductus venosus, then in the via sinistra and then in the ductus arteriosus. Functional closure precedes anatomic closure. There is a discussion of the factors which bring about respiration and the big changes in the circulation. Chapters VII and VIII are on comparative physiology, and chapters IX to XII are on the changes at birth in the human fetus and infant.

As Galen so truly said a thousand years ago, while describing the via sinistra and ductus arteriosus, the closure of these fetal channels at the birth of an animal is an even more wonderful phenomenon than was their original creation.

The book is beautifully illustrated and there is a fine bibliography. It doubtless will long stand as a classic in the literature on the physiology of the circulation. It should serve also as a beautiful example of what a man can accomplish in spare time when he is past 60 and working hard for his government—during years when his country is fighting a desperate battle for its life.

Myasthenia gravis. Por el Dr. Adalberto R. Goñi, jefe de clínica médica del Servicio sanitario de correos y telecomunicaciones. Paper. Pp. 135, with 10 illustrations. Buenos Aires: Librería y editorial "El Ateneo," 1944.

Mysthenia gravis is such a rare disease that there has been no monograph written on the subject for nearly forty years. Since 1934, when Walker discovered the striking effects of neostigmine (prostigmine) on the symptoms of myasthenia gravis, many cases have been reported and papers on research are now appearing at the rate of about twenty-five a year. Goni reports in detail 13 cases observed since 1937 in Buenos Aires and its vicinity and reviews in an adequate manner the history of our knowledge of this disease and its clinical as well as pathologic aspects. His chapter on the pathologic physiology of myasthenia gravis is published in collaboration with Alfredo Lanari, a physician who has done considerable investigative work both in this country and in Buenos Aires. This monograph is up to date, with an extensive list of references to the current literature and an adequate index. There are a few illustrations. The book, an extremly creditable volume, is, without question, the best treatise on the disease in print at the present time.

Diseases of the Nervous System in Infancy, Childhood and Adolescence. By Frank R. Ford, M.D., Associate Professor of Neurology, The Johns Hopkins University, Baltimore. Second edition. Cloth. Price, $12.50. Pp. 1,143, with illustrations. Springfield, Ill.: Charles C Thomas, 1944.

This excellent work continues to maintain its high standard. The author has eliminated the minor errors that creep into every text and has added new material. The index has been amplified extensively. This improved edition can be highly recommended for pediatricians and neurologists.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

MIXED INSULINS

***To the Editor:*—What is the consensus as to the efficacy of the mixed insulins, i. e. regular and protamine insulin and of globin insulin? Are any mixed insulins on the market as yet?** **Captain, M. C., A. U. S.**

[This question was referred to two qualified consultants, whose respective replies follow.—ED.]

ANSWER.—The combination of standard insulin with some type of delayed action insulin (protamine or globin) has been employed by all physicians experienced in the handling of severe diabetes for some years. It has been recognized that delayed action insulin, though it approached nearer the desideratum of supplying insulin for utilization at the physiologic rate than did multiple injections of standard insulin, still left something to be desired. The experience of many workers is reported in the literature of the past few years, with the consensus being that a combination of the two types of insulin works out best in those severe cases that do not regulate well on either of the insulins when used uncombined. The article by Colwell reviews the literature and sums up the present status admirably.

Globin insulin has now been given a thorough clinical trial. At first it was hoped that, because it was administered as an unprecipitated type of delayed action insulin, presumably precipitating in the tissues after injection, it would prove to be the ideal type, having a quick acting and delayed acting quotient. From clinical experience, however, it has seemed to act much like its precursor, protamine insulin.

Some of the pharmaceutical houses have been working on a mixed type of insulin, one that contains a quick action and a delayed action element. At the present time there are no mixed insulins on the market.

ANSWER.—Various attempts have been made to devise an insulin preparation having prolonged activity but also exerting a rapid effect. The ultimate aim is the maintenance of good control in the great majority of diabetic patients with a single injection daily. Protamine zinc insulin alone will control about half of all diabetic patients, the milder cases requiring 40 units or less per day. More severe cases require more rapid insulin action than is afforded by the slowly absorbed protamine zinc insulin. Good regulation may be established in many of these more severe cases by giving separate morning injections of protamine zinc insulin and of regular insulin such as protamine zinc insulin 45, regular insulin 15 or protamine zinc insulin 60, regular insulin 20, and so on. In such treatment the dose of protamine zinc insulin is usually about three times the dose of regular insulin. The results are usually satisfactory, but two injections are required, even though both are administered before breakfast.

If regular and protamine zinc insulins are mixed in the syringe or in a vial, the resultant preparation will give an intermediate type of effect (provided the regular insulin: protamine zinc insulin ratio is 1:1 or greater, since a large part of the regular insulin is precipitated by such admixture). Good clinical control may often be established by using mixtures containing 2, 2½ or 3 parts of regular or crystalline insulin to 1 part of protamine zinc insulin.

Globin zinc insulin has not yet, according to the comparative studies available, proved to offer any considerable advantages as an intermediate type of insulin. It frequently permits after breakfast hyperglycemia of excessive degree and often causes midafternoon hypoglycemia. It is completely absorbed in less than twenty-four hours, so that the advantageous overlapping effect of protamine zinc insulin is lost.

MacBryde and his co-workers have obtained results superior to those secured with extemporaneous insulin mixtures by using a single injection daily of modified protamine zinc insulin containing half or less than half as much protamine as market protamine zinc insulin (0.5 or 0.625 mg. per hundred units instead of 1.25 mg.). This market protamine zinc insulin has two components: (1) 75 per cent of any given dose is in precipitated form and is slowly absorbed throughout a period of twenty-four hours or longer; (2) 25 per cent is in solution and is rapidly absorbed, acting to control the blood sugar rise after food intake. This proportion of slow to rapid activity was selected after an analysis of 350 cases showed that it fitted the requirements of the great majority of diabetic patients. The St. Louis investigators feel that the use of variable extemporaneous mixtures has perhaps been a necessary step in developing information as to the most desirable time-activity pattern of an intermediate insulin. They believe that the use of mixtures should be discouraged because the results are irregular and the problems of mixing are confusing to patients and physicians. Since 90 per cent of a series of 110 patients were well regulated with modified protamine zinc insulin, there seems to be no necessity for the prescription of individual insulin mixtures. Other investigators have confirmed the good results obtained with market protamine zinc insulin by the Washington University group.

It seems likely that some form of modified protamine zinc insulin containing much less protamine than is present in market protamine zinc insulin will eventually completely displace the latter. There is as yet no modified protamine zinc insulin on the market. Until such a preparation becomes available it is probably best to give two separate injections, one of protamine zinc insulin and the other of regular insulin, before breakfast daily to patients not well regulated with protamine zinc insulin alone.

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RATE OF TRAVEL OF CLOT IN BLOOD STREAM

***To the Editor:*—What is the rate of travel of an embolus in the blood stream of the veins as to the time it takes to go through the right auricle and ventricle and reach the lung?**

A. P. George, M.D., Haverhill, Mass.

ANSWER.—It is assumed that the inquiry relates to the passage of a blood clot and not to that of air or fat from the peripheral veins to the pulmonary artery. Naegeli and Janker in their studies on experimental embolism with the help of a moving picture film saw that an opaque embolus, injected into the femoral vein, passes up the abdominal vena cava, hesitates for a while at the diaphragm and then shoots along the thoracic vena cava to the right auricle; even from here the embolus may come back again to the diaphragm before negotiating the transit through the heart. Certainly there is evidence of retrograde flow in the vena cava of the experimental animal. The liver enlarges in right heart failure, and in cinematographic studies of animals it has been shown that such failure is associated with regurgitation of blood from the right side of the heart into the liver. A similar temporary backflow can occur at each expiration when the liver is compressed during inspiration.

In man the rate of travel of the embolus would depend on the actual circulation time as determined by ether or decholin, on the rate and depth of respiration and on the rise in pressure in the right heart and pulmonary artery. Judging from observations in man, a sudden attack of dyspnea, cyanosis or retrosternal pain follows a sharp, tearing feeling in one of the extremities within fractions of a minute. This rate of travel is not to be confused with a slowly ascending thrombosis, which may take several days from the plantar veins of the foot to the iliofemoral segment but may break loose at any time during its progress.

DRUGS HAVING CURARE-LIKE ACTION ON MOTOR NERVES

***To the Editor:*—What drugs may be employed to produce motor paresis of isolated muscles, the drug being injected into the muscle?**

Lieutenant Commander, MC(S), U.S.N.R.

ANSWER.—Drugs having a curare-like action are magnesium, which acts on the peripheral muscles, and quinine, which in addition increases the refractory period and slightly inhibits cholinesterase. Curare itself interrupts the nervous impulse at the neuromuscular junction. Synthetic curare-like compounds such as quinine methochloride, quinine ethochloride and salts of erythroidine act in a similar manner. Onium salts in general possess a curariform action. Atropine antagonizes or prevents the action of acetylcholine, acting directly on the effector cell, plain muscle and gland cells and renders them insensitive. The local injection of 0.1 to 0.2 per cent solution of procaine or some other local anesthetic blocks the centripetal proprioceptive impulses and thereby relaxes muscular tonus, normal

and abnormal. Neuromuscular transmission is weakened so that the muscle responds better to direct than to nerve stimulation. Cold, fatigue, low potassium, excessive calcium and strong current (cathodal depression) are well known conditions unfavorable to conduction.

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RESTORATION OF BODY FIGURE AFTER PREGNANCY

To the Editor:—**A prospective mother aged 22 is interested in regaining her figure after parturition. The main problem is her breasts, which before pregnancy were large but well formed and not pendulous. They have enlarged considerably by now, the seventh month of pregnancy. What measures taken both before and after delivery will insure a return of the breasts to as nearly as possible their original state? Will the wearing of a brassière while sleeping help? Does nursing the baby tend to make the breasts pendulous? What forms of exercise, if any, are of benefit to breast uplift? Are any exercises advisable ante partum? What measures do actresses generally take to preserve their figures?**

Lieutenant (jg), (MC), U.S.N.R.

Answer.—There is little authentic information concerning the proper care of the breasts during pregnancy in order to retain their firm, normal appearance. The enlargement of the breasts is due partly to the development of the secretory acini and partly to the growth of the duct system. Proper support without compression throughout the pregnancy will prevent the excessive stretching of the tissues as a result of the increased weight and size of the breasts; it will also prevent an excessive pull on the pectoral muscles. Gentle but superficial massage of the skin with a bland cold cream may reduce the tendency toward striae.

Nursing does promote changes in the breasts, and they tend to become pendulous and flabby, rarely returning to their previous state. A properly fitting support should be worn for several months after delivery. The usual puerperal exercises are recommended, although they will not alter the tone of the breasts.

There are no special measures that actresses take to preserve their figures. The following suggestions will help: The weight gain during pregnancy should be restricted to no more than 16 to 18 pounds (7-8 Kg.). A balanced high protein diet will assure good nutrition. Daily exercises outdoors, particularly walking, will maintain good muscle tone. A properly fitting abdominal support after the fifth month of gestation will provide support for the pelvic girdle. Care at the time of delivery to prevent much separation of the abdominal muscles will assure a return of the normal appearance of the abdomen. Regulated exercises for at least eight weeks following delivery will go far to restore the figure to the normal.

DOSAGE OF TESTOSTERONE PROPIONATE

To the Editor:—**I have been administering 25 mg. of testosterone propionate intragluteally three times weekly to a vigorous man in his middle seventies who complained of inadequate energy, impaired memory for recent events and general letdown. The patient believes that he has experienced some improvement from this treatment and is insistent on larger dosage. I am hesitant to administer a greater dosage, but my hesitancy is not based on any knowledge of possible harmful effects. Is prolonged administration of testosterone in amounts of 25 mg. or more three times weekly inadvisable?**

M.D., Indiana.

Answer.—Symptoms such as those mentioned could be expected in a man of this age to be the result of the aging processes. It is also quite possible that these symptoms could be initiated to some extent by a definite decrease or loss of sex function. If the patient does not have pronounced hypertrophy of the prostate and if there is no evidence of a possible cancer of the prostate, one might be justified in increasing the dosage of testosterone propionate to 50 mg. three times weekly without fear of harm to the patient. However, it should not be administered to a man of this age for the purpose of increasing potency, which might result from doses of 50 mg.

The 25 mg. dose is usually adequate when the preparation is given for its tonic effect; this dosage is also effective in relieving the symptoms of the climacteric in younger men, in patients having hypogonadism or undeveloped testes and in castrates.

MAPHARSEN AND BISMUTH IN CEREBROSPINAL SYPHILIS—INJECTION TECHNIC

To the Editor:—**I have been using iodobismitol or sobisminol with mapharsen in cerebrospinal syphilis, including tabes dorsalis and taboparesis, attaining serologic reversal. If serologic reversal can be attained in this way is there additional advantage to be gained by using tryparsamide or malaria fever therapy? I can persuade my patients to bear the pain of the injection, but the induration of the buttock becomes extremely severe—to the point where further injections are almost impossible. Do tryparsamide and malaria fever therapy have any advantages over bismuth subsalicylate in cerebrospinal syphilis? I have not read anything on the subject since the original work of Hanzlik.**

M.D., Ohio.

Answer.—It has been the experience of the majority of syphilologists that mapharsen and bismuth do not reverse the reaction of the spinal fluid to negative in patients with tabes dorsalis or taboparesis. The blood serologic tests may become negative in tabes dorsalis without treatment of any sort, but rarely do mapharsen and bismuth cause a significant change in the blood or spinal fluid reaction of a patient with taboparesis. In other words, the experience of the inquirer is quite contrary to that reported in most of the literature during the past twenty years. In fact, mapharsen, as a rule, is less efficient in the treatment of cerebrospinal syphilis than is neoarsphenamine or arsphenamine, and the use of tryparsamide and fever therapy has become popular because their use for the patient with cerebrospinal syphilis has demonstrated their definite superiority over any of the preparations of arsenic or bismuth. Iodobismitol and sobisminol do not have any therapeutic advantage over bismuth subsalicylate.

It is probable that the local reactions to bismuth as mentioned are due to improper technic of injection. Consideration of the following factors may overcome some of the difficulty in technic: 1. The injection may be too superficial; a needle 2½ inches long should be employed. 2. Deposit of bismuth in the injection tract may occur at the time of withdrawing the needle. 3. Massage of the buttock should follow withdrawal of the needle. 4. The injection should be made with the patient lying on the table completely relaxed and not while the patient is standing or leaning over a table or chair. 5. Exercise and a sitz bath after the injection may be helpful.

INJECTION THERAPY FOR PAIN IN THROMBOPHLEBITIS

To the Editor:—**I understand that injection of the lumbar sympathetic nerves is indicated for the relief of vasospasm caused by thrombophlebitis. What is the technic? What textbook or journal is recommended for additional information on the procedure?**

Clauss B. Strauch, M.D., Hazel Green, Wis.

Answer.—Thrombophlebitis, by irritating directly or reflexly the sympathetic fibers which course along the blood vessels of the extremities, does produce vasospasm. This is manifested by a cool cyanotic extremity, with pulses diminished as compared with those on the other side; there is also a diffuse severe cramping sensation, a pain of vasoconstriction, which defies any known pattern of peripheral pathways. Under such conditions paravertebral infiltration of the regional sympathetic nerves relieves pain, decreases edema and increases peripheral blood flow. It must be emphasized, however, that not all cases of venous thrombosis exhibit these phenomena; those in the lower part of the leg are notoriously bland and are apt to give rise to embolism without much collateral vasospasm.

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CARRIERS OF HEMOLYTIC STREPTOCOCCUS

To the Editor:—**A boy aged 4 years has hypertrophied tonsils and chronic cervical adenitis. Culture of material from his throat reveals hemolytic streptococci. Should there be any restrictions against his contacts with other children, such as those incidental to attending nursery school, playing with preschool children or eating in a dining room where other young children are present?**

Daniel Haffron, M.D., Elgin, Ill.

Answer.—Group A hemolytic streptococci are pathogenic for man. A child carrying this organism in the throat is capable of spreading infection to other children, and restrictions are usually considered to be advisable although not specifically required under the department of health regulations for the state of Illinois.